THE MEDICAL JOURNAL OF AUSTRALIA

VOL. II.—13TH YEAR. SYDNEY: SATURDAY, JULY 24, 1926. No. 4.

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RECENT WORK IN CANCER RESEARCH.[1]

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Filterable Tumours.

A LARGE part of the experimental work which is being done in England in connexion with cancer research, is concerned with the experimental tumours of rats and mice and it seems desirable to make some inquiry as to their relationship to tumours as they occur naturally in the human subject. Some of these experimental tumours have arisen spontaneously. Most have arisen from the experimental application of irritants, the best known of which is crude tar, the actual carcinogenetic agent of which has not been isolated. The technique consists in applying the irritant repeatedly to a small area of skin preferably on the back of the neck which cannot be scratched readily by the animal. The adequate stimulus must continue for a considerable time which bears the same ratio to the life of the animal as does the precancerous period in a human subject when chronic irritation can be traced as a causative factor. Thus an animal may be tarred weekly for six to eighteen months before new growth appears, but once established it continues independently and the original cause is no longer distinguishable. The process may be hastened to a certain extent, thus most experimenters tar three times weekly and an initial scarification appears to place the cells in a more receptive state. A minimal time, however, appears to exist which is different for different individuals, but cannot be further shortened by any known method. The trauma applied is insufficient to cause death or violent inflammation of the cells. It would appear indeed that an attempt may be frustrated by too vigorous stimulation. The tissues may pass into a chronic inflammatory condition which appears permanently distinct from a precancerous condition. These considerations fit in well with our views of human tumours of which chronic irritation appears to be a causative factor, and suggest a fundamental similarity between the two processes.

[1] Read at a meeting of the New South Wales Branch of the British Medical Association on April 29, 1926.

There appear to be different powers of resistance or different hereditary tendencies in different animals used in experiment; thus some may develope a neoplasm within two months and others appear to be permanently resistant to that process. Again, it is well known that we may readily produce a sarcoma of rats and a carcinoma of mice, but the reverse process is difficult. Once started the tumours behave as typical neoplasms. They continue growing and infiltrating and form metastases, while the animal gradually wastes away and generally dies of inanition or an intercurrent infection in less than two months. The rapid death seems in contrast to clinical experience, but assuming that on an average mammalian tumour cells would grow and infiltrate at the same rate, a small animal such as a mouse would be completely permeated by a growth which in a human subject would still be capable of surgical removal. In the appearance of microscopic sections these tumours are said to conform to that of a typical neoplasm, but this is merely a picture of rapidly growing cells infiltrating tissues and from the experimental point of view where we begin by admitting that we know nothing of cancerous processes, such a consideration does not lead us far.

Undoubtedly the reason for the widespread use of these tumours is their convenience and the fact that they may readily be inoculated from one animal to another of the same species. In this manner a strain of tumour may be kept going continually and a supply of material is available for the carrying out of various experiments both *in vivo* and *in vitro*. In practice, however, such a tumour shows waves of virulence, so that occasionally it may die out in spite of all precautions, while experimental work is best carried out when the virulence is high. Ordinarily very little trouble is experienced with what may be described as the best tumours and their behaviour stands in great contrast to the state of affairs when a human tumour is brought in from the operating room and we attempt any experimental procedure. In fact we are dealing with educated tumours propagated in an educated animal.

Let us consider the procedure we adopt when a new tumour of a laboratory animal has arisen either spontaneously or in response to some irritant such as tar. A great many of such tumours are tried, but few are of any value, so that the tumours which have been in use for years, are seldom replaced. The procedure is to anæsthetize the animal and to remove the mass of the growth, though a recurrence always takes place. The tumour tissues are divided and inoculations made into various animals which are as closely related as possible. But as these very rarely take, autogenous inoculations are made into another part of the animal which has been operated on. This may be done twice perhaps and another attempt made to inoculate a different animal. In this way, if successful, the virulence is gradually increased to a fixed maximal value and the tumour may ultimately be transferred from animal to animal with a high percentage of "takes." Thus whatever the primary relationship to spontaneous human tumours, these experimental growths have been considerably altered by passage.

The recent work on experimental tumours by Dr. Gye has again raised the parasitic theory of cancer. When a cell becomes cancerous, it acquires quite new characters, the outstanding one being rapid and uncontrolled growth. It also has increased vitality and resistance to adverse conditions which I shall mention later, and may change in its ability to make use of sugars. From a certain point of view it may be assumed that one of two things has happened, the cell has lost something or gained something. In the former case which includes the general opinion as to the origin of cancer, it is assumed that when a cell rebels in this manner to an irritant, it reverts to a primitive or ancestral type. It loses the hereditary characters by which it has become a specialized unit in a metazoan organization. Such a theory fits in well with all the accepted ideas of tumour growth; it appears that the reversion is not so complete in some tumours which tend to produce organized tissues, while the reversion is more complete in the most malignant tumours which bear a certain similarity to one another especially in their reaction to antisera, dependent no doubt ultimately on a common ancestral chemical group.

On the other hand it may be assumed that something has been gained to account for the change. A foreign factor has arisen which stimulates a normal cell to become cancerous, and the changes in the physiology of the cell are strictly of a secondary nature. Numerous organisms have been cited as the cause of cancer, probably because various bacteria appear to live in a species of symbosis with a new growth. A growth of a mucous surface is always infected, however we dissect it. It is familiar that when an experimental tumour has become infected in this way, the organisms appear again and again in tissue cultures in spite of passage through animals until it may be necessary to let the growth die out. No doubt the same applies to invisible organisms.

Gye's supposition of a virus origin has been made to explain the outstanding phenomenon of filterability. This was first discovered in the Rous sarcoma of the fowl which was thought by many to be an infective granuloma rather than a true new growth. Gye has discovered a mammalian tumour, the mouse tumour, *S* 37, which can be transferred by cell-free filtrates, though the process presents considerable difficulties. Thus it appears that other tumours may also be found capable of being transferred in this manner.

I may mention briefly some of the properties of filters. It is generally admitted that a systematic examination is urgently needed from the points of view of the physicist and chemist as well as of the biologist. The size of the pores may be standardized and the possible existence of abnormally large ones investigated. Possibly if small laminæ of filter material were examined, an exponential law of permeability would be discovered. This law is very general in nature and from a practical point of view would lead to the possibility of a few organisms getting through a dense and apparently effective filter, provided the law still held. A filter must not

be regarded merely as a mechanical sieve which lets particles of a certain size through. Many factors operate to hinder or assist objects in passing through filters. Cells can accommodate to various circumstances, thus many tumour cells are highly amœboid in tissue culture and the possibility remains of such cells passing through dense filters in virtue of this property. In the case of bacteria it is claimed that under certain conditions they may break up or be lysed to form ultramicroscopic particles which readily pass through filters and that subsequently a normal growth may arise in the filtrate presumably reconstructed from the invisible fragments. An important property of filters which prevents objects getting through, is that of adsorption. Perhaps, indeed, filters should be measured not as to size of pores but in square feet of surface with which any medium must come into intimate contact when passing through. Hence it is seen why it is frequently necessary that a viscid fluid must be diluted to permit of filtration. Here also the paradoxical condition is encountered in which comparatively large organisms such as spirochætes may pass through readily, while much smaller or even invisible organisms may be held back. Not only organisms but gases are adsorbed on the surfaces of filters, so that under certain conditions filtration may be the means of a thorough oxidizing of a culture which has previously been kept under strictly anærobic conditions to avoid such a result. To return to the virus origin of filterable tumours: Virus is a term applied to an invisible, infective agent associated with many definite and well known human and animal diseases. By analogy we picture an organism of a nature similar to bacteria. Viewed in this light it appears that the organism must be smaller than the limits of resolution of our best microscopes and that it passes more or less readily through filters. It cannot be cultivated outside the body and is generally considered to be an obligatory intracellular parasite. The mode of infection appears according to the most recent investigations to be the inhalation of some species of spore set free by the autolysis of infected cells and the drying of the residue to a state of dust. Thus the drying of pustules and desquamation after an infective disease appear to be a necessary mechanism for the survival and propagation of its species. Such a view does not fit in with a virus theory of new growth. Neither does the painting of an animal with tar suggest in any way the mode of infection of known viruses. Variola and vaccinia have recently been studied systematically by quantitative methods and their resistance to various antiseptics determined. They were extraordinarily sensitive to permanganate of potash and are also readily killed by phenol which corresponds to the tar group of substance. On the other hand they appear to be remarkably resistant to the alcohol-ether-glycerol group of substances, so that they may be readily preserved from bacterial contamination. Gye has attempted to explain the many difficulties in connexion with the virus theory by assuming a specific factor, a chemical substance which forms a necessary link before a cell can be infected with the virus, and he has produced experimental evidence to show that two factors are present in the filtrate of the Rous chicken sarcoma. Thus the filtrate of this tumour may be rendered non-infective by treating with chloroform in a saturated aqueous solution, but when this is added to a so-called primary culture which has become non-infective from standing, a tumour may still result on injecting the mixture. Whatever the explanation may be, it does not appear to be justifiable at the present stage to assume that chloroform which is soluble to only about one-half *per centum* in water would be a lethal agent for the hypothetical cancer virus. Again after spinning either a primary culture or a filtrate in a centrifuge under certain special conditions of acidity and so forth, while supernatant fluid and washed deposit may be separately innocuous, a tumour may result on injecting a mixture of the two portions.

The presence of an accessory factor is a well-known phenomenon of infection. In tetanus, for example, it may be presumed that the cell defences must be ruptured by some chemical substance, but that the specificity and pathological characteristics of the disease are related solely to the causal organisms. But the specific factor postulated by Dr. Gye plays a much more important rôle. It not only ruptures the cell defences, but determines the species of animal which will be infected and the actual tissue which will be involved. In fact all the characters of the tumours which appear to be remarkably fixed through different generations, would be conveyed by the chemical factor rather than by the chromatin in the nuclei of the tumour cells. It is much easier to assume that the second factor is of the nature of a growth-activating substance. A growth-activating substance is derived from cells being set free by mechanical injury or autolysis. They appear to be of a nature similar to the secretion of ductless glands and serve a useful purpose in repair after trauma in stimulating fibroblast growth. Their investigation has been carried out chiefly by tissue culture method and there can be no doubt that they can awaken a dormant tissue to active proliferation *in vitro*, though a large amount of work has yet to be done on this subject. It appears from experimental work and also indirectly from clinical observation that actively growing tumour cells are richly endowed with the property of forming a somewhat similar substance which helps to maintain their own vigorous growth independent of the body and in the case of carcinomata a corresponding growth of the fibroblasts of the host to form a stroma. It is easy to imagine that growth-activating substances would abound in extracts of tumours.

There are many mysteries in connexion with filterable tumours. Carrel claims to have produced a tumour of the fowl by injecting embryo pulp and a weak solution of indol or arsenic. A spindle-cell sarcoma is formed which rapidly forms metastases and kills the host, and it may be propagated by means of cell-free filtrates.

While on the subject of filterable tumours I may consider briefly the phenomenon of bacteriophage

which has many points in common with the subject. A substance appears in the fæces of patients recovering from diseases of the dysentery group which is capable of producing a rapid and complete lysis of the causal organisms in broth cultures. A loopful of the lysed culture will produce a similar effect when introduced into a new culture and so the process may be continued in series apparently without limit. The agent which has been called bacteriophage, is found to be widely distributed and has been recovered from the water of rivers and even of oceans. It passes readily through filters; in fact this is the means of isolating it from the bacteria with which it is originally associated. Some authors regard bacteriophage as an ultramicroscopic virus which infects and destroys the bacteria. Many of the properties associated with living matter are present such as the presumable multiplication when transmitted in series, though in common with the viruses it cannot be cultured on artificial media. Only young and living bacteria are attacked. The virulence may also be increased by passage in general to a more or less fixed maximum value and a monovalent strain may be trained to attack other groups of bacteria. There is also some evidence of a particulate nature as centrifuging may cause a shift of active material.

On the other hand some authors regard it as a chemical substance, a species of enzyme which is renewed in some manner at the expense of the lysed bacteria. Bacteriophage exhibits not only the phenomenon of filterability, but in common with some so-called viruses it passes even more readily through ultrafilters. It is said to pass readily through collodium membranes which have no pores, so that we are led to suppose a chemical molecule of comparatively small size. A detailed study reveals many points of resemblance on the one hand to the problem of filterable tumours and on the other to the study of the so-called virus diseases. We appear to be dealing with a sort of intermediate stage between a chemical molecule such as a ferment and a living organism. At one moment the agent appears to obey all the criteria of life which have been formulated from the study of bacteria and cells. At another moment the properties of the infective agent appear altogether too elusive to associate with any material object unless in solution and yet the results on the organism infected are definite and constant and the agent has good powers of resistance to certain antiseptics and other adverse conditions.

A great many attempts have been made to see the invisible infective agent associated with the above conditions by using various stains but without success. The use of ultraviolet light has, however, opened up new possibilities in this direction. Mr. Barnard is steadily improving his objectives and adapting them to even shorter wave lengths. The causal agent of pleuro-pneumonia has been photographed at one stage of its life history. Fortunately protoplasmic structure shows a considerable degree of optical differentiation or selective absorption to ultraviolet light, so that the enormous advantage is gained of examining material in a living state and eliminating the process of fixation and staining which always lead to many fallacies. The object can usually be seen by dark ground illumination and focussed; the small focal depth, however, presents great difficulties. Failing this small droplets of mercury are focussed. The ultraviolet focus is found by trial and error for the first time and its distances measured from the visible focus for future use.

The future will no doubt decide what relation the filter passing agents bear to the cancer problem. Perhaps the actual cause will be found among these minute organisms and it may be possible to photograph it. Or perhaps when present they may turn out to be merely adventitious, living with the new growth in the same manner as bacteria.

It is considered that an important or crucial discovery may be made at any moment. I shall leave for the moment the question of whether the fundamental property of a neoplasm is represented by an infection or a perverted physiological change and consider the cell. The cancerous cell is a very real entity which can be seen and studied experimentally, and in any cure of or production of immunity against cancer it appears to be quite sufficient to deal with the cells as we find them.

Tissue Culture.

A great advance has been made in the study of cells by the discovery of means to grow them *in vitro*, the so-called tissue culture. Cells may be kept under observation on a hot stage and various experiments performed or different substances added to the growth medium. The conditions are certainly not exactly the same as in the body, but it has been found that within limits the behaviour in tissue culture is a reliable criterion of the subsequent behaviour *in vivo*. For example tumours which are very malignant *in vivo*, generally grow luxuriantly *in vitro* and many reactions to antisera and lethal agents appear also to hold under the two conditions. Certainly the influence of reaction of the body as a whole is removed, but much valuable information can be gained by studying tumour cells by themselves or with various other tissues in this way. The science is yet in its infancy and it is not possible to formulate any general laws of growth or experimental truths apart from the particular conditions under which the cells are grown.

Like most new discoveries the technique was at first very different, but it has been greatly simplified and cells can now be grown in pure serum from any convenient animal, provided that the hydrogen ion concentration is kept at approximately the correct value, a condition to which the cells appear to be very sensitive. By this method growth may be readily obtained and is fairly reliable and no undue amount of work is needed in preparation. Many older methods presented so many difficulties before growth could be obtained that little time or scope remained for experimental work. Indeed many experimental conclusions which had previously been

arrived at, have been found to be unreliable or completely wrong, the results obtained depending on unintentional variations in the medium of growth. It is not known what substances are necessary for growth, but no doubt a simple saline solution with sugar added, having a suitable hydrogen ion concentration will ultimately be used.

Mottram has done some exact work on the optimum carbon dioxide and oxygen tension for growth allowing various mixtures of gas in jars to diffuse into the cultures. He finds that it is best for the tension of carbon dioxide to be slightly higher and that of oxygen slightly less than in the blood, a condition which probably obtains in normal tissue fluids. Lumsden has found that tumour cells can survive twenty-four hours in anærobic culture and Mottram finds that they can continue to grow under nearly anærobic conditions or completely anærobic conditions, if sugar be added. The remarkable vitality of tumour cells can be conveniently demonstrated by tissue culture methods and the effect of various destructive agents investigated and compared with normal tissues which may be conveniently grown together with the malignant cells in the same droplet. During my stay I investigated the action of ultraviolet light on normal and malignant tissues in this manner and published it in *The Lancet* of May 1, 1926. For work of this kind a glass cover slip may be used, provided that it is thin. A rough estimate of penetration was made by means of a quartz spectrograph and it was found that about 25% of the energy of wave-length greater than 300 was transmitted (the so-called near ultraviolet) and about 3% of the energy below this wavelength, a region which is generally considered to contain the physiologically active components probably because of its ready absorption by protoplasms. It was found that in every case normal tissues were killed by a much shorter exposure than the malignant cells, thus the carpet of epithelial cells growing from kidney was killed in about ten minutes, while it required eighty minutes' exposure to produce a similar effect on a mouse cancer. It was thus possible by growing normal and malignant cells together in the one droplet to kill the former by an exposure which produced no noticeable effect on the latter.

Some authors use the cessation of mitosis as an end point to determine the effect of an agent, but mitosis is undoubtedly influenced by factors which are yet unknown, and its occurrence is irregular in serum culture. A very convenient end point is the death of all cells which have migrated from the fragment and adhered to the cover slip at the time of exposure. These cells are in an especially vulnerable position. There is seldom any doubt about the death of a cell once the appearance has become familiar. When observation is continued on a hot stage all amœboid movement ceases and changes in the protoplasmic granules occur in the space of a few minutes. The function of the cell membrane is lost and changes occur due to the intake of fluid. The cells become swollen and globular in outline and later changes of disintegration become manifest. Changes are best observed twenty-four hours after the actual exposure when the above effects are clearly manifest and appear very striking if a control growth which has been shielded during exposure, is present on the same slide. A convenient record is made by taking two photographs at intervals of a few hours; the absence of any change in shape or position leaves no doubt as to the death of the cells.

A similar high resistance is noted to other agents. Normal cells may be killed by three hours' exposure to a specimen of radium which requires twenty-four hours to kill malignant cells. Similarly a high vitality is noted when malignant cells are stored in the cold room or exposed to heat, though I think some valuable information would be gained by more exact work in this direction. When the medium of growth is unsuitable similar results obtain. Malignant cells resist infection well in tissue culture and I have seen cells survive for three weeks in the same droplet without refeeding or opening up the wax, in spite of a heavy bacterial infection and presumably some accumulation of waste products and exhaustion of food substances. At the end of this period the hydrogen ion concentration is not greatly altered, but probably some carbon dioxide has diffused out and has been replaced by a non-volatile product such as lactic acid. Thus it appears that when dealing with malignant cells *in vivo* it is hopeless to attempt to kill them outright; the endeavour must be made to cooperate with the natural defences of the body brought into play by suitable stimulation.

Many problems await to be investigated by tissue culture methods. Problems connected with the nutrition and multiplication of tumour cells may be readily investigated, for example, by adding different substances to the medium of growth. The reactions to various sugars may also be investigated and the extent to which cells may be trained to make use of new sugars. The problems of growth-activating substances have not by any means been worked out, but there can be little doubt that similar factors may play a very important part in the growth of tumours *in vivo* and the accompanying stroma reaction. Then there is the question of balance of tissues, the process by which epithelial and mesoblastic tissues remain in equilibrium. It is known, for example, that a contracting scar may be arrested and remain supple and vascular if epithelial cells be grafted on to the surface of the granulation tissue. This again seems a promising field for cancer research. The process does not always appear to be well defined when tissues are grown *in vitro* but very little can be said at this early stage. I shall leave the extremely important reactions of antisera for the following section on immunity.

Immunity.

I was privileged to work with Dr. Lumsden during my stay in England. His work on immunity in connexion with the experimental tumours of rats and mice may prove to be one of the most important advances recently made in cancer research. It has

been known for a considerable time that a state of immunity can exist to experimental tumours; after spontaneous absorption an animal is immune to subsequent inoculations of that neoplasm. Barlow has shown that such a state of immunity can exist in an animal cured with radium. Russ has inoculated animals with two tumours and cured one with radium. After a few days the other untreated tumour was found to have become stationary or have retrogressed, but apparently the experiments were not continued and brought to a conclusive stage.

Lumsden has worked chiefly with the Jensen rat sarcoma and a mouse cancer M63 of the Imperial Cancer Research Fund, investigating the problem by tissue culture methods which as I have noted give reliable information at least to a first approximation. He tried to make antisera by injecting the tumours into various animals and tested their sera on *in vitro* cultures. Many previous attempts have been made to make a specific antiserum, but without success and it has been concluded that it is impossible to differentiate between malignant and normal cells in this manner owing to their similarity. Only one or two injections, however, were made. Lumsden gave a dozen or more over a period of some months. The resulting serum was then found to kill the same tumour cells rapidly *in vitro*. On placing a drop on a growing culture and observing on a hot stage the changes already described could be seen in the space of a few minutes; all movement ceased, the outline became ragged and the granules irregular in size and distribution. Later a swelling and rounding out of the body of the cells was noted. Some of the most active antisera appear to kill and fix the cell almost before changes appear as if a steam jet had been played on the slide, but subsequent observation reveals the absolute immobility.

It may be thought that the properties of the serum were antirat or antimouse rather than antitumour, but normal cells were found to survive quite well beside the dead malignant cells even in the case of a carpet of epithelial cells from kidney which is one of the most delicate tissues to grow. The normal cells also continued to multiply freely, so the property was not one of antigrowth. The reaction appeared to be truly specific, although the case of an inoculated tumour is not quite the same as that of a spontaneous tumour, a difficulty which obtains with all experimental growths. Nevertheless the reaction was very striking and quite dependable, a contrast to all other destructive agents which affect normal tissues first. There also appears to be an overflow immunity from one malignant tumour to another. I mention this briefly as the subject has not been published, but it may represent a very important discovery. It indicates a change (associated with malignancy) apart from mere rapid growth which may be detected by serological methods. It indicates also an extensive avenue of research by which the cause of cancer may be investigated by determining what fundamental alteration of chemical groups are associated with the malignant change.

Considerable difficulty was experienced in applying the results *in vivo*. Injections of antiserum were made into the blood without success. Finally by injecting directly into the tumour and applying constriction so that the antiserum could not escape rapidly into the general circulation a successful result was obtained. As the technique was improved in nearly every instance an animal could be cured which would otherwise be condemned to death in a month or six weeks. The results were clear and decisive and subsequently the animal was free from recurrence and immune to further inoculation. There is, therefore, justification for the use of the word cure.

The following experiments are of extraordinary interest and were described by Lumsden in *The Lancet*, September 12, 1925. Rats were inoculated with tumours in two feet and these were allowed to grow to a reasonable size so that there could be no doubt that they would continue to spread. One foot was then treated with antiserum and when the treatment was successful, the untreated growth in the other foot grew normally for about four days and then became stationary and rapidly retrogressed, leaving a scarcely visible scar or more often a perfectly normal foot even when the skin had been tightly stretched over a large tumour. The animal had been cured and had acquired an immunity sufficiently powerful to deal with an amount of healthy malignant tissue at least equal to that of the tumour treated. The reaction was provoked by the absorption of products of disintegration of the treated tumour, since when it was amputated before four days had elapsed, no immunity resulted. The tumour in the other foot grew and ultimately killed the animal. A similar failure occurred when an abscess developed and the products of disintegration were able to escape.

Various other agents were tried as controls including constriction alone and constriction with various antiseptics. Very little success was obtained corresponding to the great relative resistance of tumour cells to non-specific agencies *in vitro*. Occasionally by happy combination of circumstances the treated foot was cured and then in every case the other untreated foot healed spontaneously. The effect appears to be due to absorption of products from injured tumour cells. It is not directly due to such products, since the untreated tumour grew normally for four days, while the treated tumour remained more or less inflamed and swollen. It is a vital reaction with the body cells which have been trained in this way to deal with other actively growing tumour cells. The inoculation of dead cells does not appear to have any effect on a tumour-bearing animal, the destruction must not have proceeded too far. It seems that cells must be brought to one particular stage between life and death at which they can act as an effective antigen. This stage may be reached by any convenient means. Possibly in the rare instances in which a human or animal tumour is cured spontaneously, the necessary stage is reached through some vascular disturbance, but the margin

is narrow and a spontaneous cure correspondingly rare. It appears that by the use of a specific antiserum the desired state may be reached more conveniently and with greater reliability.

It appears that in practice we should aim not at killing a tumour cell, but at reducing it to this particular antigen stage whereby it can train the body to deal with other actively growing cells. In other words no attempt is made to destroy cells directly; there must be cooperation with the natural defences of the body if a successful result is to be obtained. We may turn again to tissue culture methods to investigate the state of the cured animal. Its immunity is found to be complete for two or three months after treatment, but the actual time limit has not been determined. To obtain decisive results with the animal serum and to test its state of immunity inoculations of tumour tissue were continued for some months in order to develope a hyperimmunity and finally large intraperitoneal injections of five or six cubic centimetres were given and were completely absorbed in a few days. It was found that the serum did not give the same reactions as when a different animal had been inoculated, yet its cellular immunity was effective and lasting. A reaction may be obtained on these lines by which the state of immunity could be tested, for example in a patient treated by radiation by means of the *in vitro* cultivation of surviving tumour cells with the human serum and leucocytes or lymphatic gland tissues. The question of immunity seems to be definitely settled for these experimental tumours and within limits an animal can be cured at will. Let us consider whether we can apply these results to spontaneous human tumours. The subject of a new growth appears to have in his tissue fluids substances which are favourable to the growth of malignant cells; he is in what might be called a "negative" state of immunity. Is it possible to alter this to a "positive" phase of immunity in which the visible growth not only disappears, but any existing outlying nodule or secondary deposit is effectively dealt with, so that a real and permanent cure has been effected?

It has been shown that it is sufficient to deal with about half of the mass of the growth or less, but a large tumour seems to absorb products of disintegration—the substances circulating in the blood which must precede immunity—like a sponge before the body tissues can react with them. The cure of one tumour in an animal cannot be effected if one or more other tumours of very large dimensions exist, that is when the additional tumour mass is about three times the size of the treated tumour. Once immunity is established, it seems that an almost unlimited amount of tumour can be dealt with as in the case of the rats which were given large intraperitoneal injections of virulent material. It seems reasonable to try the effect of antisera on human tumours when part of the growth is readily accessible. Lumsden proposed to inject antiserum into the arteries leading to a growth and to tie the veins in place of constriction. No doubt it would take some time to perfect the technique, for the antigen stage admits only a narrow variation. It is, however, a hopeful line of investigation.

It may be useful to consider the bearing of the question of immunity on radiation treatment. I am especially interested in this subject, but recognize that if the percentage of cures of malignant disease is to be improved, there must be close cooperation not only with the natural defences of the body, but also between the serological expert, the radiologist and the surgeon. There is some evidence that it does not essentially matter by what means cells are brought to the antigen stage, any agent which could be effectively applied and controlled, would probably be equally good. For deep inaccessible growths radiation has the great advantage in this respect. Russ has indicated an effect in his experiments on animals with two tumours in which one was treated and the other retrogressed spontaneously. The effect is probably similar to that of the antiserum. It may be that in treating a patient with X rays or radium we should aim not at killing the cells, but as in the animal experiments at reducing them to the antigen stage which can stimulate the production of immunity. Before considering the possibilities in detail, I would like to make a few general remarks about radium and X rays and also of the recent work which I have seen regarding their action on cells.

Radiation.

It is believed that all radiant energy is represented by one phenomenon and different properties are matters of different wave length. Thus light rays have a relatively large wave length compared with X rays, while ultraviolet light has an intermediate wave length value. There is much experimental work of great interest in connexion with ultraviolet light, but it has little bearing on the cancer problem. Ultraviolet light may be conveniently applied to tissue cultures, but it is of little use in a growth *in vivo*. The penetrating power is poor so that it cannot reach the tumour, being absorbed in the horny layers of the skin though in virtue of its known therapeutic action it must reach the superficial capillaries of the skin. X rays on the other hand have the enormous advantage of reaching any deep situation on account of their penetrating properties. The two main sources are radio active substances and the X ray tube in which a piece of metal is caused to emit rays by what amounts to a very intense bombardment. I shall try to compare from a practical point of view the respective merits of these two sources. I have mentioned that radiant energy is of a great variety of wave lengths, but the properties of X rays themselves vary considerably, especially of penetrating power according to wave length. The soft X rays which are easily absorbed, are of comparatively large wave length and lie next to the ultraviolet light, while hard X rays which have great penetrating power, are of much shorter wave length. Sometimes it is more convenient to speak of frequencies than of wave length. As all radiant energy travels at the speed of light it is found that a large wave length has a low frequency, while a small wave length has a

high frequency. They are reciprocals. Many people consider that we should think in terms of frequency instead of wave length, as the former represents a more fundamental property of radiation. Another manner in which X rays may vary, is that of intensity and in general any source gives a fairly wide range of wave lengths of different intensity in different regions. For example there are certain series or groups of spectral lines called the K, L, M and so forth, radiations which are characteristic of the element emitting them. Thus in order to know what X rays are being used not only the total intensity must be known, but the intensity or amount present of each wave length.

If radium is considered along these lines, it will be seen that it will give an enormous amount of energy, say in a thousand years, but we have no control over the process. It goes on whether the element be used or not. In actual practice it is feeble. To treat a malignant growth requires twenty-four hours' exposure as against twenty-four minutes with an X ray tube. If the distribution of the energy as to hardness or wave length be examined, a wide range is covered. Thus there are the K, L, M characteristic radiations of the element radium, the latter representing extremely soft rays. Radium also emits certain very hard radiations, that is of very short wave length, much harder than it is possible to obtain with the most powerful X ray plant. They can be detected through twenty-five millimetres of lead, though greatly diminished in intensity. In this respect they are much more powerful than X rays which can barely be detected through two millimetres of lead. But the intensity is nevertheless small; it represents only 1% or 2 % of the total radium radiation. It might be thought that these very hard rays have some special therapeutic property, but this is very doubtful as they pass through the human body without any appreciable absorption; in consequence they cannot do much work there. Their action has never been investigated. It would be necessary to screen a source of radium with about eight millimetres of lead and certain other substances and to expose the patient for about a month if we wish to know the action of the hardest γ rays. The action of radium is due to the soft components of approximately the same wave length as is used in ordinary X ray work. But besides the true radiation which is generally known as γ rays, radium shoots out material particles, α and β rays. The β rays may be used therapeutically on surfaces, but they do not penetrate very far and have not much application on massive growths. A far more important fact is that γ rays in common with all other X rays have the property of generating secondary β rays in the depths of the tissues as they pass through. There is probably very little difference in the action of radium and X rays, in practice; the choice is one of convenience. Certain growths are very conveniently treated by inserting radium needles and leaving them for about twenty-four hours, but the action is at best uncontrolled and owing to the small percentage of hard rays which cannot be screened off, the applicators are very dangerous for all those who look after them. In fact pathological changes can generally be detected after two or three months' work in a radium clinic. The X ray tube and generator give the great advantage of control of the radiation. The total energy may be increased to any convenient value so that a new growth may be treated in twenty-four minutes. With the use of metal tubes it may soon be possible to do it in four minutes, so that a large number of patients may be treated in twenty-four hours as compared with the number of patients who can be treated with radium in the same time. Not only can the total intensity be controlled, but also its distribution in different wave lengths. Thus a soft tube can be used to differentiate a kidney in a skiagram or to prevent action spreading too deeply when a surface condition is being treated. On the other hand a deeply placed growth is treated by hard rays, being attacked at different angles, the so-called "cross-fire" system, so that the growth receives a full dose without any one area of the skin being unduly exposed. Thus for the majority of purposes X rays can replace all the effects of radium in a much more practical and easily controlled form. Moreover, the worker can be completely protected by the intelligent use of a moderate amount of lead.

When the effect of radium and X rays on tissues is considered, it is found that they have the general properties of an irritant. Tissues may be damaged and ultimately killed and like all irritants a small dose causes stimulation. A portion of the circumference of a round tumour is given a small dose; later a bulge appears in this region due to increased growth. Radiation also appears to have a certain specific effect on dividing tissues by interfering with the process of mitosis. This is well observed in tissue culture. Different types of reaction have different latent periods before any effect is noted. It thus appears that the action is a complex one. It appears to depend on the vital activity of the cell, so that any interference with its nutrition leads to a diminished reaction, even in the case of venous congestion which was supposed to induce some local reinforcement of the radiation by "scattering" from the blood pigment. When the rate of injury is low, a cell appears to counteract the effect or to keep pace with the damage and repair it. As the intensity is diminished, the effect diminishes rapidly and beyond a certain stage disappears. This is from an experimental point of view. It is known from clinical experience that a cell may become cancerous through very slight doses of radiation extending over a large number of years. Nothing is known of this process, but a shorter cumulative effect has been studied in the case of the rat skin. This effect had a time limit of twenty-four days; a reaction was reinforced when a moderate or large dose was given within that period. When the initial dose had been small, it acted as a desensitizing dose causing a diminished reaction.

The experimental study is one of great complexity, but the clinical applications are becoming much more dependable as knowledge is gained in this direction. Radiation is a convenient means of stimu-

lating or depressing the action of tissues (the fundamental action of all therapeutic agents). Its virtue is its penetrating power, so that every cell may be reached as when a drug is conveyed by the blood. Nevertheless the action can be localized to any extent desired. Radiation has been used for many years in the treatment of tumours and the dosage and technique are being continually improved. Uncertainty is, however, the keynote of the process. Frequently relief can be given and occasionally an inoperable growth clears up as if by magic, but the percentage of success is still very low. It appears that dosage will always be a fairly exact and critical matter especially in view of the immunity experiments, but it is reasonable to think that the other variable wave length may have something to do with the uncertainty.

Differential Action.

The hypothesis of differential action assumes that a particular biological effect is related to one particular region of the X ray spectrum, so that different wave lengths would have different effects. An apparent differential effect appears with hard and soft rays, but this is due to their penetrating power; the soft rays are heavily absorbed by the skin and easily cause a burn.

Various workers have investigated hard and soft rays experimentally. By increasing the voltage on an X ray tube the percentage of hard rays is increased and it is possible to filter off the remaining soft rays by a screen of copper or aluminium. To use soft rays only the screen is removed and a low voltage used. Working on these lines Russ considered that he had found some evidence of differential action, but later experimenters take the view that none exists apart from the phenomena of varying penetration or absorption which in the case of living tissues varies in a regular manner with the wave lengths. The hard or soft rays thus obtained are not monochromatic or of one wave length. They are an assorted mixture of mostly hard or mostly soft as the case may be. To investigate truly monochromatic rays about 99% of the energy must be sacrificed, a fact which has no doubt deterred many workers.

The X ray spectrometer is an instrument in which by reflecting the rays from a crystal a spectrum is obtained similar to that obtained when light is passed through a prism. For every angle of reflection there is a beam of truly monochromatic X rays, though the intensity is so small that it would appear impossible to produce obvious effects. By exposing eggs or more correctly the allantoic membrane or breathing organ of the chick embryo this very feeble beam was found to destroy the tissues completely with an exposure of less than seventy-two minutes. The effect occurs only at certain well defined wave lengths, although equal doses were given throughout, so that this would be true differential action. The destruction took place with less than 10% and more probably with less than 1% of the energy that would be required, had an attempt been made to produce the effect with ordinary mixed rays. Thus the differential action which is observed with the X ray spectrum, would appear to be masked by a species of antagonism when ordinary mixed rays are used. The enormous loss of total energy does not prevent us from obtaining striking effects, if other wave lengths are removed which tend to antagonize the reaction. I saw some work in London indicating the same kind of antagonism between ultraviolet and visible light. The stimulation of a muscle was many times greater with ultraviolet alone than when ultraviolet and visible light were both used. A rough exploration of the X ray spectrum, however, indicates qualitative as well as quantitative differential action. The remarkable destruction of the membrane took place at three regions, some of the intermediate wave lengths appear to have no effect at all, but at many regions there appeared a species of inflammatory reaction, a raised hypertrophic area corresponding to the beam of rays which passes through the spectrometer slip. When these hypertrophic reactions were sectioned, they presented widely different pictures according to the region of the spectrum from which the specimen had been taken. In one case the growth was of a myxomatous nature, in another the epithelium was enormously hypertrophied and had invaded the mesoderm like a carcinoma. In yet another an enormous infiltration with leucocytes was noted. It is possible that the properties of true monochromatic rays are so different from mixed rays that all the present applications of X rays should be reinvestigated on these lines.

If such a fact is proved to be true, what bearing will it have on the cancer problem? I have already discussed a very hopeful possibility, the possibility of producing the antigen stage which will insure not only an apparent cure but a true immunity. There is also the possibility of monochromatic radiation of suitable wave length injuring the cancer cells in the same way that the membrane of the chick embryo was destroyed. Very great energy is not required if the antagonism of other wave lengths is removed and complete destruction is not to be aimed at.

Perhaps monochromatic radiation will prove in this way to be a convenient and precise means of producing the desired effect and exceed the value of mixed radiation in the same way that the specific antiserum surpasses the non-specific agencies in the case of the rat experiments.

NON-SPECIFIC IMMUNITY.[1]

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I MAY divide the discussion of non-specific immunity into three parts:

I. Is there such an entity as non-specific immunity?

[1]Read at a meeting of the Victorian Branch of the British Medical Association on March 3, 1926.

II. What is the nature of this immunity?

III. What are its therapeutic possibilities?

Is there such an Entity as Non-specific Immunity?

Specific immunity depends upon specific antitoxins or antibodies which are efficient in their action on the antigen used in their production and on no other. They are not absorbed when administered orally.

Non-specific immunity depends upon all the factors concerned in the maintenance of tissue vitality and function. These are not absorbed when administered hypodermically.

The following experiment is a concrete illustration. A series of guinea pigs was tested with the Schick test under gradually increasing doses of diphtheria hypodermically exhibited. Normally the guinea pig gives a positive Schick reaction. The intradermal dose of toxin used was $^1/_{33}$ minimum lethal dose and the toxin was added to successive animals hypodermically in 0·1, 0·2, 0·3, 0·4, 0·5, 0·6, 0·8, 1·0 and 1·2 of a minimum lethal dose.

From 0·1 to 0·6 minimum lethal dose a positive Schick reaction was obtained in two days exactly as in the controls. The following table gives the other results.

Number.	Weight in Grms.	Schick Test Dose. m.l.d.	Hypodermic Injection of Toxin. m.l.d.	Results.
6	250	$^1/_{33}$	0·6	Schick reaction in two days.
7	250	$^1/_{33}$	0·8	Schick reaction in four to five days.
8	250	$^1/_{33}$	1·0	No reaction; died in four days.
9	250	$^1/_{33}$	1·2	No reaction; died in three days.

The Schick reaction definitely excluded all specific antitoxin.

No antitoxin being present, the results were entirely due to non-specific factors. The resistance offered to the toxin was the full expression of the natural immunity of the guinea pig.

Therefore, the natural immunity of the guinea pig depends upon its non-specific resistance. And as a matter of fact all natural immunity is due to the non-specific factors. The Schick reaction is clearly a tissue reaction and it is obtained only when no antitoxin is present to protect the tissues by neutralizing the toxin injected.

What are the forces concerned in this reaction?

1. Being a tissue reaction the tissues themselves are vitally concerned and this brings into action the endocrine hormones necessary for resistance and repair.

2. Being a toxic invasion the vasomotor system is affected and the dilatation of blood vessels with the increased blood supply shows that the blood antienzyme resistance is being increased as required.

3. Both of these factors depend on the condition of the animal's vitality. When 0·6 minimum lethal dose was injected, the vitality of the animal provided the necessary resistance to give the Schick reaction in two days, but when 0·8 minimum lethal dose was given, it failed to react till between four and five days after injection and 1·0 minimum lethal dose not only abolished the reaction, but brought vitality to an end.

To sum up: (i.) All specific antitoxin was excluded.

(ii.) Therefore results obtained were due to non-specific factors.

(iii.) The resistance offered was the full expression of the animal's natural immunity.

(iv.) Therefore, the natural immunity of the animal depended entirely on non-specific factors.

(v.) The Schick reaction is a tissue reaction and depends upon endocrine stimulus and antienzyme blood resistance, both of which in turn depend upon the vitality of the animal.

(vi.) Therefore non-specific immunity, natural immunity and general vitality depend upon the same factors and stand or fall together.

What is the Nature of this Immunity?

The answer to this question has been rather anticipated in the conclusions derived from the experiment.

Whatever resistance may be offered by man or animals to invasion by toxic enzymes or toxic proteins must be actually or potentially present in them physiologically. The capacity to resist disease which is present in rude health when compared with that found in a person with low vitality speaks for itself. The normal functions carried on with vigour are a much greater protection from infection than the same functions on a lower level of vitality and power. Thus it is recognized that to a certain extent idiosyncrasies apart, the presence of a vigorous vitality indicates the possession of more of the resistance to disease than that possessed by those with a lower level of vitality.

This suggests that the agents producing the vitality and the means of resistance to disease are identical and that both are in the actual possession of the patient.

This resistance is not a specific antibody, for it exists in man and animals in which no antigen is present.

This being so, the resistance normally present in man or animals must be a non-specific immunity varying in its capacity with the vitality of the patient.

An animal with a natural immunity to a certain organism loses more or less of his natural resistance

to that organism in proportion to the reduction of his vitality by cold, hunger, hæmorrhage or any other debilitating agent.

This resistance to infection whatever its nature may be, is a normal condition and is ready for instant action on infection. Like all other natural functions, it is also capable of development either physiologically or pathologically and that development is rapid as these functions are already in constant action and only require an increase in potency and not the formation *ab initio* of a capacity only potentially present.

The specific antitoxins take time to develope. Their administration to the patient supplies him with what he cannot supply himself without a delay which would materially lessen his chance of recovery. Till he produces or receives the antitoxin his only defence is the non-specific and in mild cases this is sufficient without the presence of the antitoxin. As non-specific immunity is so closely identified with general vitality, an examination of the physiological processes concerned in digestion, absorption, assimilation and tissue metabolism may throw light on the subject.

This is a protein problem and everywhere it resolves itself into the toxic enzyme and the toxic protein. In digestion the enzymes present are pepsin and trypsin and both are toxic to proteins. Trypsin is the more important of the two and it is a very far reaching enzyme. The very method of its secretion by the pancreas suggests that trypsin is dangerous to all tissues. The gland produces trypsinogen which in itself is innocuous and which only becomes active when united with the enterokinase of the intestine.

In its own sphere trypsin is a powerful digestive, but in the blood and in all tissues its action is toxic. Trypsin acts in an alkaline medium and therefore in blood and on tissues in the living subject.

The fact that trypsin is capable of action on any protein which may be introduced into the digestive tract, shows how wide is its range of action. And these proteins are all foreign proteins which are being prepared for entrance into the blood. They vary from time to time according to the diet, but vary as they may, trypsin by its definite action on them all, breaks them up and reduces them to their simplest forms. Pepsin and trypsin thus find themselves amongst the more or less digested materials absorbed from the intestinal tract and passed into the portal vein. If injected directly into the blood the contents of the portal vein are toxic to the patient and one could scarcely expect it to be otherwise when the sources of the materials contained in it are recognized.

All the elements absorbed from the intestinal canal are present there and when the enzymes, the proteins in every grade of lysis, the bacterial flora with their toxins and other digested contents of the canal are considered we do not need to look further for the toxic character of the portal vein contents.

Volumes have been written on autointoxication from the intestinal tract and it is clear that if the patient is not to be poisoned by his food and its accompaniments, there must be some immunizing process in constant operation capable of neutralizing the toxic contents absorbed and of preparing them for all the functions required by the tissues of the body.

This immunization process is seen in the increased dosage of aperients required to produce reaction when frequently repeated and to all other agents which produce reaction in the digestive tract under the same conditions. The liver furnishes this perennial supply of materials capable of so transforming the toxic portal contents into non-toxic blood contents. By its secretions it maintains a constant immunizing process on all the toxic materials passed through its channels. The portal vein pours its contents into the liver and they become intimately associated with the secreting cells of that organ. As they pass in they are toxic, but when they emerge into the blood they are transformed into non-toxic materials ready for all nutrition, defence and repair.

What has become of their toxic character? The antipepsin and antitrypsin of the blood supply the answer so far as the enzymes are concerned. The liver secretions have acted on the enzymes, so that on one side of the liver they are enzymes and on the other side they have become antienzymes.

This antagonism is exemplified in the coagulative power of the blood. Blood with trypsin in it will not coagulate, but if sufficient antitrypsin be added, the coagulative power is restored.

Again the lowered functional capacity of the pancreas in diabetes with its impaired secretion is reflected in the lowered antitryptic serum content which is seen not only in the patient's liability to staphylococcic infection, but also in his feeble resistance to that organism. This antienzyme content of the blood not only resists the growth of all organisms with their heterologous enzyme action, but on it also depends the bactericidal, complemental and opsonic power of the blood. That is, the toxic enzyme of the portal vein has become not only non-toxic, but in the blood is the defence against all enzyme action. So we may say that as is the range and capacity of the liver by the action of its secretions on enzymes passing through its channels, so is the range of action and capacity of the same secretions in the blood to antagonize efficiently all toxic enzymes there, whether these are physiological or pathological in their origin. And these secretions are available not only to meet external toxic materials, but also to increase the antitryptic content of the blood in infections which have found an entrance into the blood stream. In the liver the secretions of that organ are concentrated, but in the blood stream they are diluted in the whole volume of the blood. The concentration in the liver is necessary for intense local action, but in the blood stream the secretions are diluted and combine with other elements for the full defence of the economy.

Amongst these other elements are the endocrine hormones for every tissue in the body and the com-

bination of these two provide a toxic and a tissue immunity for all tissues.

With other gland secretions and the food content of the blood they are passed out with the lymph into the intercellular spaces where they become closely associated with the various tissues in the metabolic processes which the tissues undergo. The building up of tissues from the food provided and their proteolysis go on concurrently in the same lymph medium.

The tissue enzymes break up the tissue protein and produce toxic enzymes and toxic proteins. The antitryptic contents of the lymph are directly hostile to the tissue enzyme and by their antienzyme action on the tissues which are bathed in the lymph, they provide a definite antienzyme resistance to the tissue enzyme. Concurrently there is the endocrine action on the tissues stimulating them by the chemical hormones in the lymph and giving tone and vigour through their action on the sympathetic system. This raises the tissue resistance to the tissue enzyme.

Any enzyme or proteolytic product of tissue metabolism passed out into the lymph is neutralized by the antienzyme and complemental content of the lymph and its further toxic action is inhibited. Thus tissue lysis is resisted and nutrition is facilitated and the harmonious action of these factors makes for vigour and health. The endocrine and antitryptic contents of the serum resist all organisms and thus the more efficient their physiological action becomes, the greater the protection they afford to the patient.

So that what has been said in the earlier part of this article can be reaffirmed, that a vigorous, healthy subject by the very efficiency of his tissue reaction is more refractory to infection than one on a lower plane of vitality and that his health and his immunity are due to the one cause.

Any deficiency of either endocrine or antitryptic action would leave the tissue enzyme and its toxic products free for unrestricted toxic action by the tissue enzymes and toxic proteins with consequent tissue lysis and loss of tone and power.

Other glands such as the spleen and mesenteric add their quota to the lymph and play their own part in metabolism. Altogether with the endocrine and antitryptic contents of the blood they form the non-specific defence of the body.

This defence is not specific in the sense that to any one organism there is produced a specific antibody, but by various combinations the constituents group themselves so that an efficient resistance may be made to antigens whether in natural or acquired immunity.

Toxic Proteins.

All the proteins which pass through the digestive tract, whether of animal or vegetable origin, are foreign proteins and they have to be so disintegrated and changed in their character that from foreign and toxic proteins they may be fitted for use in building up instead of breaking down the tissues.

The digestive enzymes more or less prepare them for these functions and they and the enzymes pass into the portal vein. The contents of the portal vein are not fit for direct absorption into the blood and a reversal of their action is required before they can provide food for the tissues. Here as with the enzymes the change takes place in the liver as they pass through on their way into the blood. Whether this is accomplished by the liver providing an immune body for them (as for all protein tissues injected) which unites with the complement of the blood to produce a complete lysis or whether by some other means the same end is secured, one cannot say, but the result is the same by whatever means it has been brought about. The proteins when they reach the blood are fit for use in building up the tissues. That the immune body-complement action does take place is strongly suggested by the leucocytosis which accompanies the absorption of protein, thus perfectly reproducing the leucocytosis following bacterial invasion. And this leucocytosis is regulated in its intensity by the amount of protein present in the meal which is being digested and absorbed. The specific action of the liver on all substances passing through it is exemplified in its glycogenic function. The sugar is changed into glycogen which can be stored in the liver and tissues and used as required instead of producing a polyuria till it had been excreted.

The reaction of Van den Bergh in jaundice confirms this with regard to bile. The reaction is obtained in the obstructive type of jaundice, but not in the hæmolytic. The reason is that in the hæmolytic type the blood has to pass through the liver, the action of which causes the difference.

The Therapeutic Value of Non-specific Immunity.

Here then we have Nature's reservoir of material prepared for the maintenance of nutrition, integrity, function, defence and repair of every tissue and the means whereby it is reticulated to the outermost cell.

Thousands of cases treated in the last twenty-eight years prove that the non-specific toxic and tissue immunities in the serum are absorbed when orally used and reproduce in the patient the results which they were intended for in the animal supplying them. The limits of their action in the animal are the only limits in the results obtained in the patient. Physiological sera produce physiological effects and immune sera produce their own special results showing the development of the non-specific content of the serum. These results depend on the antigen used in the production of the serum.

Not only in the theory, but also in the practice of the use of non-specific resistance there emerges the fact that the maintenance of the normal tissue tone and the defence against antigen invasion are due to the same factors.

Thus the oral use of sera, normal and immune, produces definite results when no infection is present, for it supplements the patient's natural

forces and thus increases the efficiency of all his functions. So complete is this transference that whatever non-specific resistance the animal supplying the serum possesses to any infection, is passed on to the patient.

Thus a tuberculous patient's tissue reaction to serum from an animal normally resistant to tubercle bacilli is not inhibited by the tuberculosis present. The toxic immunity present in the serum due to its special antitryptic content neutralizes the infection present and enables the endocrine and other secretions to fulfil their functions unhindered.

This constitutes natural immunity and this resistance to tuberculosis is to be found normally in the horse and the sheep and can be transferred to the patient by the oral use of their sera.

In immune sera the non-specific resistance is developed, so that not only is the endocrine and antitryptic content of the serum increased, but the balance of both is adapted to the defence of the tissues which are specially toxophile to the infection present. This is what makes antidiphtheria serum the most complete representative of non-specific resistance.

Diphtheria toxin has two distinct actions; it paralyses tissues and is a vigorous proteolytic. The action of the first is on the endocrine system, more especially the adrenals, and the second directly attacks the antitryptic content of the blood. The adrenals and the antitryptic factors in the blood are each so fully occupied in their own defence that neither can help the other. This constitutes the gravity of a diphtheria infection and it calls for the utmost reaction possible of the elements involved.

An antiserum produced under such circumstances possesses not only the antitoxin in high degree, but also the non-specific defence of every tissue in the body which is directly or indirectly affected by the toxin present.

The non-specific endocrine and antitryptic contents of the serum are largely augmented. The non-specific resistance is normally in constant operation and thus has only to adapt itself to the diphtheria toxin. Thus when the antitoxin titre is two hundred units per cubic centimetre, the non-specific content of the serum has reached its limit and so two hundred units per cubic centimetre has been adopted as a standard for the serum used orally and locally for its non-specific action.

The action of the streptococcus on the tissues shows it to be an analogue of the paralytic element in diphtheria toxin and that of the staphylococcus is an analogue to the proteolytic action of the same toxin. Thus the therapeutic effect of antidiphtheritic serum on these two organisms is a perfectly natural feature of the non-specific action of the antiserum.

Normally the endocrine and antitryptic secretions resist the septic organisms and the immmunization to diphtheria serves only as a stimulus to the utmost development of these non-specific factors and with these serum contents developed to the *n*th degree, why should they not be capable of their full antiseptic and repairing action on wounds? The direct application of the antiserum to the raw surfaces applies the materials it contains to the very tissues requiring its aid and assistance. If it does this when used orally, how much more when applied directly instead of being diluted in the whole volume of the blood.

When serum therapy was first introduced there was to be a specific antiserum for every disease. The dream has not been realized, but in non-specific immunity lies a realization of the dream.

Non-specific immunity may be obtained to all agents toxic to the tissues whether a specific antitoxin or antibody is produced to them or not, so that instead of guessing amongst the glands and endeavouring to imitate Nature in her combinations, we can ask Nature by the injection of the antigen present to produce in her own laboratory her own combination to meet the situation.

We have only scratched the surface of the new therapeutics.

Summary.

1. There is a non-specific immunity physiological in normal serum and developed in immune serum according to the antigen used in its production.

2. This non-specific immunity is contained in the alimentary system.

3. It consists of the various secretions concerned in digestion, absorption, assimilation and tissue metabolism and control.

4. Non-specific immunity provides a toxic and a tissue resistance to all pathogenic organisms.

5. Non-specific immunity can be transferred to patients by the oral administration of the serum. Hypodermically exhibited its therapeutic effects are not obtained.

6. Natural immunity depends entirely on this non-specific resistance. Anything which lowers general vitality, equally lowers both natural and non-specific immunity.

7. Thus general vitality, non-specific immunity and natural immunity are all alike due to the same series of vital processes. Thus all of these are available to the patient by the oral exhibition of the serum.

THE NON-SPECIFIC USE OF ANTIDIPHTHERITIC SERUM.[1]

By T. S. CAMPBELL, M.B., Ch.B. (Glasgow),
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IT is with no little trepidation that I venture into a controversy that has been present in Victorian medical circles for many years. It is I think about twenty-eight years since Dr. Paton first introduced the treatment of various septic conditions by the oral administration of diphtheria antitoxic serum.

[1] Read at a meeting of the Victorian Branch of the British Medical Association on March 3, 1926.

Dr. Paton has given all his attention to the subject for more than a quarter of a century and he has elaborated what is to the ordinary man a rather complicated body of theory in regard to the mode of action of the serum. On the theory I can express no opinion. I confess that it carries me out of my depth. But I have used Dr. Paton's treatment in my practice for two and a half years and I have come to believe that his results are correct and that similar results can be obtained by any man giving the treatment a reasonable trial.

To some extent the defence of serum treatment is a defence of empirical medicine. But it is a question whether empirical medicine is in need of any defence.

The use of cinchona in malaria antedated for a long time the discovery of the plasmodium and ipecacuanha in dysentery and mercury in syphilis were used successfully before the discovery of the amœba and the spirochæte. The intelligent use of empirical treatment demands two things, sound judgement and a knowledge of what I might call the natural history of disease. It is only by a sound knowledge of what will be the normal course of an illness that a man may judge whether or not his treatment is modifying that illness and a medical man's ability as a physician will depend on a combination of this knowledge with a judicial mind.

It is from this point of view that I venture to bring forward some of the results I have had in my practice from the use of antidiphtheritic serum.

In my first few cases I used the serum as a last resort. My first case was that of a woman with a lobar pneumonia at the base of the right lung. She was suffering from typical pneumonia and it being typical pneumonia, she was likely to get well. But she had nothing to spare. Her breathing was laboured, it was difficult to get her to sleep and she had a pulse varying between 114 and 124. On the fifth day pain suddenly developed in her left side and there was evidence of involvement of the base of the left lung. There was no sign of resolution on the right side, but the breathing became much worse and the pulse rate increased. I had to face another week with the chances of recovery tremendously lessened. I used serum as an experiment and the result fully justified Dr. Paton's claims. I commenced the use of serum about twenty-four hours after the second lung became involved. The pulse then was varying between 128 and 132 (under full doses of stimulant) and the respiration rate was between 48 and 52. In another twenty-four hours the respirations had been reduced to 36 and the pulse rate varied between 100 and 108. The second attack lasted for five days and during that time there were typical signs of consolidation of the base of the left lung, but all cause for anxiety ceased for she had the general appearance of a patient with pneumonia with very little toxæmia.

My second patient was a girl nine or ten years of age. She had pneumonia involving the whole of the left lung with a very severe toxæmia. The nurse in charge rang me at 10 o'clock one night to report a pulse rate of 160. The child had two injections of camphor during the night and next morning the pulse rate was 140, but the child was semi-comatose. As the whole lung was affected there seemed no hope of a crisis and the child was given serum with nothing more than a pious hope that it might do good. She had one hundred cubic centimetres of serum each day for eleven days. During all that time there was no sign of resolution. The lung was so dull to percussion that I put a needle in at various parts, but found no fluid.

With each day the child's general condition improved until at the end of ten days she lay in bed playing with her dolls and asking for mashed potatoes for dinner and yet the lung was still solid. She had still rapid respiration, was breathless if she moved in bed, but she had ceased to be toxic. The chart showed a daily fall in the temperature and pointed so definitely to a favourable termination that I stopped the serum because of the expense of the treatment. In forty-eight hours the temperature had risen and by next day reached 39·4° C. (103° F.). The child had developed the little short cough of empyema and pus was found in the chest. I believe that the serum had been stopped too soon.

I may be excused if I report a third case in full. I was called out one night to see a girl of seventeen who had given birth to a child with no one in attendance. I sent a nurse round next day who reported that there was a complete tear of the perineum. Next day the patient was removed to hospital and arrangements were made for a general anæsthetic on the following morning, that is on the third morning after the birth of the child. The girl looked very ill when she was placed on the table. The temperature was 39·2° C. (102·6° F.) and the pulse rate 120. When I examined her I found a complete tear extending well up into the rectum. Pus was pouring from the uterus over the wound. The uterus was gaping so that the hand could be inserted right up to the fundus. The cervical wall was so friable that a volsellum forceps could not hold in it. I cleaned up the wound, put in some stitches and packed the whole thing with a mixture of 1 in 2,000 "Acriflavine" with serum. The patient was given fourteen cubic centimetres of serum every three hours. Next morning the temperature was 39·4° C. (103° F.) and the pulse rate 140, but the improvement was continuous and on the thirteenth day after admission the temperature and pulse rate were normal all day. Eighteen days after admission the perineum looked so healthy that I was able to do a complete repair and to get a perfect result.

These three cases were from my point of view experimental and very careful observations were taken. I am willing to admit that no one of them proves anything nor do all three combined. But they all illustrate a deviation from what one expects to be the normal course of a disease. The same type of result is obtained repeatedly until one reaches the stage of being able to predict results with reasonable certainty. That is surely sufficient foundation on which to base practice.

Among my case records in the last two years are two septic pneumonias, two mastoid infections, two

cases of kidney infection, one case of iritis and several carbuncles and septic throats, all treated by serum apparently with good results.

One of the cases of septic pneumonia followed extraction of teeth. A pure culture of *Streptococcus viridans* was isolated from the sputum. The illness ran a course for many weeks. On two occasions the serum was stopped, but each time the temperature and pulse rate rose so alarmingly that it seemed necessary to resume treatment.

The kidney infections were both in elderly people, one in a woman of seventy. Both patients had rigors before treatment by serum was commenced and in both there was a return to normal health in a remarkably short time.

In the two mastoid infections it was impossible to recommend operation, in one because both ears were affected and in the other because a severe bronchitis complicated the condition and the patient was much too ill to make an operation possible. Both patients made a complete recovery under serum treatment, the second after treatment for three weeks.

I have a record of three or four cases of carbuncle. The treatment has been successful in all the cases, but not uniformly so. One case was in a woman of ninety. In this case I used serum both internally and locally with a very rapid cessation of pain. In another case after two sleepless nights the patient got freedom from pain after the third dose of serum. But some of the other patients reacted much more slowly. In all, however, the toxæmic condition had disappeared after forty-eight hours of treatment.

I think that I have seen a more spectacular result in carbuncle under treatment by colloidal manganese, but I have not been able to get uniform results by manganese and I think serum treatment is more reliable.

Cases of iritis do not come much within the scope of the general practitioner, but my one case is worth recording. The patient was a young man whom I had sent to the Eye and Ear Hospital for treatment. The cause of the iritis was obscure, but the weight of evidence was apparently in favour of some septic teeth as the origin of the trouble. These teeth were extracted, but the gums remained unhealthy looking.

The patient continued his attendance as an outpatient at the hospital, but came down to see me one afternoon with the pain in the eye most acute. It was not his day for attending hospital and I had to try to give him some ease. I wrote him a prescription for serum to be used as eye drops and another bottle to be taken internally. He returned next morning with very little sign of inflammation round his eye and his own statement was that half an hour after he commenced treatment, the pain disappeared as if by magic. This patient had a note to appear at a post-graduate demonstration at the hospital a few nights later.

By way of confirming my result I had asked him to take one hundred cubic centimetres of serum each day for three days, in the meantime continuing his eye drops. When he appeared at the demonstration I believe that no sign of iritis could be detected.

I have no explanation to offer for the result. The rapidity of the action suggests that it was a local action due to the instilling of the serum into the eye. It is certain that many cases of conjunctivitis can be relieved more quickly by the local application of serum than by any other known treatment.

Serum as a local application has not such a wide field as in its internal use, but some of the results obtained are quite as phenomenal and it would seem as if any explanation of the mode of action must explain both the local and the general results. Broadly speaking, I think it can be claimed with safety that serum applied to an inflamed surface will relieve the inflammation. It is on this basis that I have carried out local treatment and it is on the results of a large number of cases that I base the statement. My test case was one of *erythema nodosum* with painful nodes on both legs and a moderate degree of fever. I chose the most inflamed and most painful node and applied a dressing of serum covered with jaconet. The other nodes were untreated. Next morning the node which had been treated, was least painful and it had become paler than the others. The test seemed to indicate a fair degree of absorption through the skin.

I have used the serum as eye drops in several cases of conjunctivitis and always with good results.

Within the past few months I have used it in three children suffering from colitis. Two of the cases were acute, the third an exacerbation of a chronic condition. In all three patients the bowel was washed out and fourteen cubic centimetres of serum injected. The serum was retained without any trouble. It not only gave relief from the constant straining, but seemed to improve the general condition of the patient within a very short time. I think that the greatest number of injections found necessary to effect a cure was four.

I hesitate to encroach on the domain of the specialist, particularly of the throat and nose specialist, but I find good results from serum in many throat cases. Several children in my practice get relief in recurring sore throats by two or three paintings of the throat with serum. In two patients from whom adenoids had been removed and had grown again and were causing deafness, I got the mother to pack the nostrils at bedtime with cotton wool soaked in serum and in each case the mother reported a very rapid improvement in the condition.

One of my most remarkable cases was in an old lady of seventy-nine who had a very severe attack of *herpes zoster*. I saw her one morning about fifteen hours after the appearance of the eruption. She had had rather a distressing night and I prescribed a salicylate mixture and a dusting powder. When I saw her next day she was pitiful in her exhaustion. She had had a night of the most acute pain. The eruption had spread and parts of it were dark and necrotic looking. I think that I prescribed serum as an application merely because it was on my mind and I knew of no other effective treatment. Three or

four layers of gauze were soaked in serum and placed over the affected part. The old lady's description of the result was that it felt as if someone were lifting the pain right off her side. The application was renewed as it was found necessary and no other treatment of any kind was used, for there was no more severe pain and no post-herpetic neuralgia. I tried to repeat this result in a second patient with herpes. The application eased the pain in a similar manner though not so dramatically, but the patient had a good deal of neuralgia after healing had taken place.

I shall give one more of my experiments with serum used as a dressing. I had occasion to see a man with a very severe electric burn involving the whole of the right arm from fingers to shoulder. The man had been treated as an out-patient at hospital for a week before I saw him. He had a furred tongue and a temperature varying between 37·6° C. and 38·8° C. (100° F. and 102° F.). The discharge from his arm was so profuse that it soaked through three towels in the course of a night. I gave him first serum by the mouth and as a dressing for the arm. The toxæmia quickly cleared up, but the dressing of the arm with serum became rather a problem because of the amount of serum necessary and the time taken to remove the old dressings and apply the new. To overcome the difficulty I got Rocke, Tompsitt and Company to make me an ointment containing about 30% of serum with lanoline and olive oil. Using this I was able to leave a layer of gauze untouched over the whole surface and to apply the ointment over this with a brush. The dressing of the arm took only a fraction of the former time. The ointment kept the arm free from smell and healing took place remarkably quickly.

I understand that Rocke, Tompsitt and Company have put this ointment on the market under the name of "Serol." I have used it since, in two patients with burns and the results are quite as good as in my first patient.

I have quoted only cases in which the diagnosis was reasonably certain and the result seemed to point to the serum as the determining factor in the cure. There are numbers of cases in a general practice in which an exact diagnosis may be impossible or perhaps it would be more exact to say a diagnosis is made but cannot be confirmed or proved.

I have the chart here of a patient who came into hospital in the first stage of labour. She had a temperature of 37·4° C. (99·4° F.) and a pulse rate of 100 and her general appearance indicated that some abnormality was present. When the placenta was delivered it was found that almost a quarter of it had been detached for some days and it was evident that the rise in temperature and pulse rate was due to a sapræmic condition. When I saw the patient on the following day the temperature was normal, but the pulse rate was 108 and she had a restless look. I ordered fourteen cubic centimetres of serum every three hours as a precautionary measure, although I could find no definite cause for alarm. In less than twenty-four hours that patient had a phlebitis extending from the saphenous vein across the front of the thigh almost as far as the back of the knee. Yet there was no rise of temperature. The pulse rate varied between 80 and 96; the vein was very tender and nodular and was bright red along its whole course. Local treatment with ichthyol was used in addition to internal treatment with serum. In less than three weeks no nodules could be felt and there was no sign of tenderness. The patient left the hospital in three weeks from the day of admission and the temperature had not reached 37·2° C. (99° F.) from the morning following the birth.

All that one can say is that a result like this is contrary to what one usually finds. That is all that can be said of any of the cases, but when these results multiply, one feels justified in ascribing them directly to the action of the serum.

If the serum does give these results, then it gives them in a manner which differs fundamentally from other forms of treatment. It appears to act by increasing the patient's resistance to the infection. It changes a toxic condition into a non-toxic one, while the disease is still running its course.

I should like to mention one or two points in regard to the administration of the serum. Dr. Paton in giving serum used teaspoonful doses. The serum I have used is that made by the Commonwealth Serum Laboratories and sold in one hundred cubic centimetre bottles. I have found it necessary to give doses of fourteen cubic centimetres every three hours to get results. One bottle of the serum lasts roughly for twenty-four hours and at the end of that time it is generally possible to determine how the patient is reacting. The serum is put up in two forms—with and without antiseptic. I fancy that I have obtained better results with the serum containing the antiseptic, but of this I am not certain.

The criticism has been levelled at Dr. Paton's treatment that it is in a similar class to Hicksonism. My practice is not in any way a serum practice. I have prescribed serum exactly in the same way as other drugs, so that the patient is unaware of what is being ordered. When a patient has to pay ten shillings and sixpence for a mixture that lasts only twenty-four hours, one does not prescribe it unless for some very good reason.

I think I can safely say that I have prescribed serum only when I felt it unsafe not to do so or where I felt certain that the saving of time in an illness justified the expense to the patient.

One warning I should like to give. In a dangerous infection which is reacting to serum treatment, it is of the utmost importance that the treatment be continued until the temperature has been normal for about forty-eight hours.

It is with a great deal of diffidence that I bring forward this series of cases. My natural place is among the inarticulate section of the profession who rarely appear at medical meetings and never by any

chance in print. I consider it a bad habit to bring forward successful cases, for most of us learn more from our failures which rarely see the light of day or the publicity of a medical meeting. And the successful case might have done as well under different treatment or with no treatment at all, for the *vis medicatrix naturæ* is still as powerful as ever. My only excuse is that I am defending not my own treatment but another man's and that I believe that the fundamental fact is that this treatment is not only so much better than others for certain conditions, but that it is different.

The progress of medicine is to a large extent the scientific investigation of clinical observations.

The cases that I have reported are selected from a very much larger number in my practice. In the nature of things the great majority of cases in practice are unsuitable for reporting. In many of my cases I was convinced that serum helped the progress of the case materially, but I had no data with which to convince another man. I only held my belief because of my experience of disease.

It is impossible to estimate the number of cases in which a little more or a little less resistance on the part of the patient makes all the difference between life and death.

Reports of Cases.

TABES DORSALIS WITH ANTERIOR HORN DEGENERATION.[1]

By KONRAD HILLER, M.D., Ch.B. (Melbourne),
Honorary Physician, Melbourne Hospital, Melbourne.

A MALE patient, aged fifty-seven years, an invalid pensioner, gives a history of having suffered from a primary syphilitic chancre twenty-eight years ago. He was not treated at that time, but has received intensive treatment during the last ten years. The therapeutic measures have included both intravenous and intramuscular injections.

Twenty-six years ago the patient noticed shooting pains in his legs and also found that his toes caught on the ground and that he had to lift his feet higher when he walked. Twenty years ago his legs became weak. He was not sure of his steps and if he took his eyes off the ground, he fell. At this time he complained of some severe pain in the lower part of the abdomen. The pain was so severe that it made him vomit. Eighteen years ago his hands became weak and wasting of the muscles gradually supervened. Fifteen years ago retention of urine occurred. Since that time it has occasionally been necessary to pass a catheter, though there have been periods of up to twelve months' duration in which he has passed urine with freedom. For seven years the patient's sight had been failing and he has occasionally suffered from transient diplopia. Seven years ago he was in hospital with a fractured leg and he has walked on crutches ever since. For five years he has complained of severe burning pain around the abdomen, if he takes a bath. At one period he suffered from "influenza" and his signs and symptoms became worse. For three years he has suffered with severe pains in the back of the neck, in the hands and the lips which had been tremulous for eight years and which are now characterized by a more severe degree of tremor. He has also suffered from an attack of dyspnœa of a spasmodic character accompanied by a cyanosis and loss of voice.

[1] The patient described herein was shown at a meeting of the Victorian Branch of the British Medical Association on May 28, 1926.

At the present time the patient is unable to walk without crutches or without springs on his boots. He is able to use his hands to a slight degree, he is unable to hold a cup. He complains of occasional shooting pains. He had complete retention of urine and a catheter was passed four months ago. He usually passes urine every hour or so. His bowels act regularly, there is no incontinence. He is losing weight, he sleeps badly and his appetite is poor.

On clinical examination he appears flushed, his lips are tremulous. His pupils react sluggishly to light and accommodation. His systolic blood pressure is 158 and his diastolic pressure 104 millimetres of mercury. The volume of the pulse is poor and the blood vessels are thickened. The urine is acid, its specific gravity is 1020, it contains neither albumin, sugar nor pus cells, but a few casts. The heart, lungs and abdomen are apparently normal. Movement of the spine is restricted by weakness, there is no rigidity.

On examination of the central nervous system the meninges appear normal, Kernig's sign is absent, there is no stiffness of the neck and the cerebro-spinal fluid is normal. The cranial nerves are normal except for the tremor of the tongue and lips. Examination of the motor system reveals a fine tremor while the patient is at rest; this becomes gross and resembles an intention tremor on attempted movement. Some fibrillary twitching is present. The small muscles of the hand and foot together with the *tibialis anticus* and the peronei muscles are wasted. Power is diminished, especially in flexion. The deep reflexes are absent. The plantar reflex is flexor in type. The abdominal reflexes are absent. Double foot drop is present and the hands are held in a claw-like position. In regard to sensation the sense of position, sense of movement and of deep pressure are absent. Sensation of pain is generally diminished especially on the ulnar border of the hands. Sensation of heat, cold and of light touch are not grossly affected. The presence of intention tremor interferes with all tests of cerebellar function. The patient is emotional. His reaction time is slow. His speech is slow and monotonous and his voice is high pitched. His writing is large and almost illegible. The serum and cerebro-spinal fluid have each been examined on two occasions by the Wassermann test and no reaction has been obtained. No increase of cells or of globulin was found in the cerebro-spinal fluid. A positive result was obtained on application of the acetic anhydride test. The optic discs are a little pale. The blood urea figure stands at twenty milligrammes.

PROBABLE CASE OF RAT BITE FEVER.

By T. W. SINCLAIR, M.D., D.P.H.,
Medical Officer of Health, Melbourne.

M.R., AGED thirty-seven years, employed as a rat catcher by the Melbourne City Council, was bitten by a rat on the back of the middle finger of the right hand over the proximal phalanx on January 7, 1926. The wound was washed, a dressing applied and it subsequently healed. On January 25, when the dressing was off, he knocked the finger which had been bitten and it became inflamed and painful. He was referred to his medical attendant who made two incisions on the back and front of the proximal phalanx and ordered foments to be applied. Under this treatment the condition improved and the wounds showed signs of healing by February 4. On February 10 red blotches and streaks were noticed on the right arm and his temperature was 38·8° C. (101° F.). There was some glandular swelling and tenderness in the right axilla and side of the neck. By February 15 the finger was well, but the redness on the arm was present though the temperature was normal. His condition improved and he was able to resume work on February 22. On February 26 there was glandular swelling and tenderness in the right axilla and side of the neck and a pink, pimply rash had appeared

on the body, especially on the chest and abdomen, along with pains in the legs. The temperature was normal.

On the suspicion that the condition was one of rat bite fever, he was given 0·4 gramme of "Novarsenobillon" intravenously at the Melbourne Hospital on February 26 and thereafter his condition improved so that he was able to resume work on March 2, since when there has been no recurrence of symptoms. No attempt was made to examine the patient's blood for the spirochæte, but the prompt and permanent clearing up of all symptoms after one dose of "Novarsenobillon" seems to confirm the suspicion that the case was one of rat bite fever. It is well known that a single dose of "Salvarsan" or of one of the allied arsenobenzol preparations acts almost as a specific in cases of this disease. This report is forwarded as I am not aware of a similar one having been recorded in Australia.

GRANULOMA TROPICUM.

By LANGLOH P. JOHNSTON, M.B., Ch.M. (Sydney),
Honorary Dermatologist, Sydney Hospital;
Honorary Dermatologist, Saint Vincent's Hospital, Sydney.

THE patient, a man, aged twenty-one years, came from Noumea, complaining of ulceration of the anus of eleven years' duration. He had undergone many forms of treatment and in 1919 skin grafting was carried out without any benefit resulting. He gave no history of syphilis and on submitting the blood serum to the Wassermann test a result described as +++ was obtained.

The appearance of the ulceration is seen in the accompanying illustration. The granulating area was at least fifteen centimetres (six inches) in length and 3·75 centimetres (one and a half inches) wide. It was situated in the gluteal cleft and extended an equal distance in front of and behind the anus.

A diagnosis of syphilis was made and treatment with arsenical preparations was undertaken. In all six injections of arsenic and eight of mercury were given, together with large doses of iodide of potash. No improvement resulted. Obviously another cause had to be sought. Although no Leishman-Donovan bodies could be found, it was decided to give sodium antimony tartrate. A dose of 0·03 gramme (half a grain) was given intravenously and within a week the lesion had healed. Four more injections were subsequently given. The patient now suffers from stricture of the anal orifice.

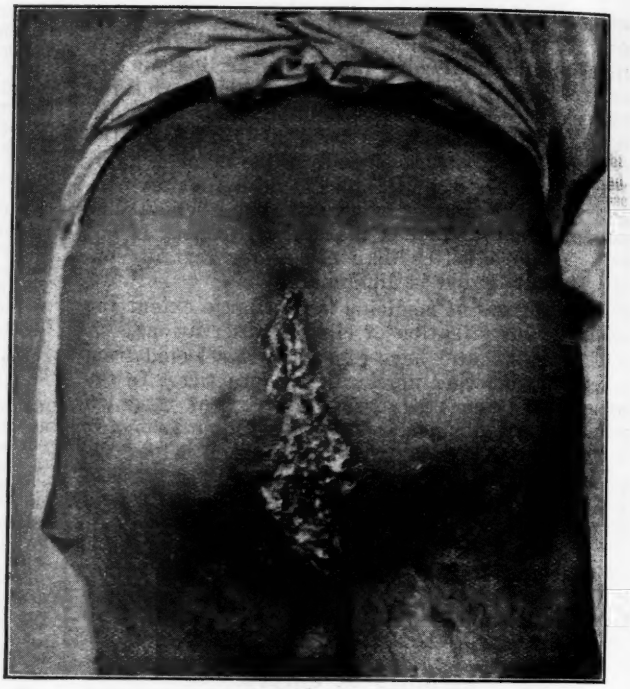


FIGURE I.
Showing Lesions before Treatment.

FIGURE II.
Showing Condition after Treatment.

DIABETES MELLITUS TREATED BY RAW PANCREAS.

By L. J. J. NYE, M.B., Ch.M. (Sydney),
Atherton, North Queensland.

IN *The British Medical Journal* of March 14, 1925, Hollins described his successes in the treatment of *diabetes mellitus* by raw pancreas. This was followed by confirmatory reports by Young (March 28), Dunn (April 4), Kelly and Griffiths (May 16), while Harrison and Graham have reported their failure to obtain results in patients who were at that time being treated with "Insulin." These latter criticisms carry little weight until further investigations are made, for Hollins has distinctly stated in his reports that for some unknown reason raw pancreas was not effective in patients who had previously been treated with "Insulin."

In a recent issue of THE MEDICAL JOURNAL OF AUSTRALIA I also noted that Dr. Horn, of Brisbane, had successfully treated two patients and I therefore decided to test its efficiency on a patient who was under my care.

The patient, a married woman, aged sixty, had been suffering from *diabetes mellitus* for some considerable time and was in a very low state of health. She was being nursed by her daughter,

a trained nurse, who had been paying strict attention to her diet and who also took the readings of the sugar estimation tests shown below without having any idea of their significance.

The results of previous diabetic test dieting had shown that the patient had a very low carbohydrate tolerance and for the purpose of testing the efficiency or otherwise of the raw pancreas, she was given a strict diabetic diet with the addition of thirty grammes of white bread and eight grammes of sugar. This amount, representing twenty-three grammes of carbohydrate, was given at the midday meal and the urine for testing was voided two hours later. A daily quantitative sugar estimation was taken for five days on this standard diet without pancreas; then seven grammes of raw pancreas were given at breakfast and at lunch for the following five days and so on as indicated in the chart. The quantitative test was Eve's modification of Gan's test.

The specific gravity of the urine is taken as soon as it is passed. It is then shaken up in a warm "Thermos" flask with seven grammes of yeast. The flask is kept in a warm place and the specific gravity is again taken on the following morning. It will be found to be less because all the sugar is converted by the yeast into carbon dioxide. Every degree of specific gravity lost corresponds to 8·866 grammes per hundred cubic centimetres (one grain per ounce) of glucose.

By a study of the accompanying chart it will be seen that the results in this one case are not quite as satisfactory as has been described by other observers, for the sugar has not been entirely cleared up by small doses of the gland; still the improvement has been so evident that it certainly appears to have a distinct place in the treatment of diabetes. It is possible that its indiscriminate use in all cases without careful observation may lead to disaster, for since Cowles first described his original successes in 1911, other skilled investigators failed to obtain uniform results. Cammidge suggests that the cause of these divergent results with raw pancreas may be that it contains two fractions, one in connexion with the utilization of sugar and the other with deposition of glycogen. The sugar utilizing portion is rendered inactive by the gastric juice, so that when the glycosuria is due to defective storage, it should have beneficial effects, but when it is due to impaired sugar utilization, it is of little avail.

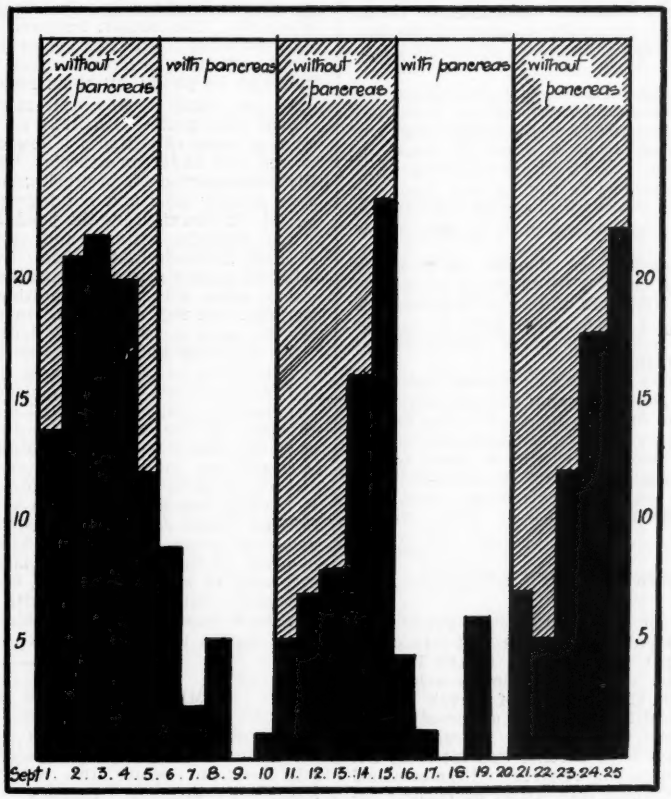


Chart Showing Results of Raw Pancreas Administration in Dr. Nye's Patient.

In my patient the improvement in her general health while having pancreas is so apparent to her that she is determined to continue the treatment for the rest of her days if necessary.

At first she thought the cure was much worse than the disease, but now she "manages" it quite well and would not consider the alternative of an injection with a needle.

Reviews.

OSLER'S MEDICINE.

IN the second volume of the revised edition of Osler's "Modern Medicine," the high standard set in the first is fully maintained.[1] It will be especially welcomed because it happens to include so many diseases about which knowledge has greatly advanced since the publication of the previous edition. This particularly applies to diseases caused by protozoa, those due to physical, chemical and organic agents and the deficiency diseases.

The first two hundred pages deal with diseases of doubtful or unknown origin. Dr. Poynton in his article on rheumatic fever makes a very strong indictment against the *Diplococcus rheumaticus* as being the ætiological factor, so strong indeed that the reader is left with the feeling that the disease only barely comes in under the doubtful category. Apart from the ætiological aspect Dr. Poynton, as would be expected, has produced a most admirable essay on his subject.

Those in New South Wales and Queensland who wrestled so strenuously with dengue fever last summer, often as victims themselves, will be interested in Dr. Coleman's account of the malady.

Though there is little that is new to be written on the subject, Dr. Beardsley contributes so graphic a clinical picture of smallpox with excellent illustrations, that it should be widely read by the many practitioners in this country who have never seen a case of the disease, but upon whose ability to recognize a sporadic case, the fate of this largely unvaccinated community may at any time depend.

Many readers of Dr. Strong's rather voluminous account of amœbic dysentery will be surprised to find how many varieties of the protozoa have been found to infect the human bowel. A large amount of valuable information is supplied, but it might well have been more condensed. In discussing treatment Dr. Strong supplies a very full account of the various methods available and one schooled in dealing with this disease will welcome some of the alternatives offered him when harassed by resistant cases, but the novice will look in vain for a clean line of attack.

The malarial fevers are exhaustively discussed in an excellent article by Dr. Charles Craig. While most authorities will agree with him that the heroic doses of quinine sometimes administered are unnecessary and at

[1] "Modern Medicine, Its Theory and Practice," edited by Sir William Osler, Bart., M.D., F.R.S., Re-edited by Thomas McCrae, M.D., Assisted by Elmer H. Funk, M.D.; Volume II.: Diseases of Doubtful Etiology *et cetera*; 1925. Philadelphia: Lea and Febiger; Sydney: Angus and Robertson, Limited. Royal 8vo., pp. 901, with illustrations. Price: 42s. net.

times even dangerous, many will feel that he errs in the other direction in suggesting that after the disappearance of acute symptoms the dose may be dropped from two grammes (thirty grains) daily to 0·65 gramme (ten grains). It is worthy of note that this small dose which Dr. Craig suggests, should be continued for three months to eradicate finally the established protozoa, is one-third less than he recommends to be taken as a prophylactic dose by those exposed to infection. He makes no reference at all to the use of arsenic in the convalescent stage, a drug which played an important part in the scheme of treatment issued by the British War Office during the Great War.

Other protozoal diseases dealt with, trypanosomiasis and Leishmaniasis, are fortunately not seen in Australia. Such excellent results were obtained in tegumentary Leishmaniasis (oriental sore) by exposure of the sores to X ray emanations in Australian hospitals during the Syrian campaign, that it is surprising to find that Dr. Growell in his account of this disease mentions only treatment by tartar emetic given intravenously especially in view of the fact that he warns the reader that a few cases of sudden death have been ascribed to the treatment.

Charles Wardell Stiles, Ph.D., D.Sc., has contributed the entire section upon diseases caused by animal parasites. He has clearly a unique knowledge of his subject and has compiled a monograph that seems destined to rank for long as a standard reference to which all will turn when confronted with an unfamiliar infection of this kind.

Under the title of "Diseases due to Chemical and Organic Agents" there is much that is quite new and all is extremely interesting.

Alexander Lambert's facile pen depicts in a really fascinating way the many and varied effects of alcohol on the human body and the victim of this type of indulgence would be astonished to read of the many rôles he may be destined to play. The suggestions as to treatment are most valuable and convincing.

Pellagra, beri beri, scurvy and rickets appear under the heading of "Deficiency Diseases" and the articles have had to be largely recast in order to incorporate the results of the extensive investigations that have been carried out in these fields. Special reference should be made to the admirable account of pellagra given by Dr. Jenner Wood, based upon experience gained in treating over two thousand patients with the disease.

A PRACTICAL WORK ON GYNÆCOLOGY.

In the second edition of his handbook on gynæcology Dr. Bethel Solomons has enlarged on the first edition of six years ago and brought the work up to the level of present knowledge.[1] The chapter on menstruation has gained by the embodying of the work of Novak and O. Franke and the account of the disorders of menstruation represents up-to-date ideas presented in a concise and practical form. In dealing with chronic endometritis, Dr. Solomons simplifies the subject by reducing all the so-called types to one form—the chronic interstitial or chronic infective type. In regard to this long standing "itis" of contention he will have most present day pathologists on his side. In connexion with treatment, he strongly deprecates the "indiscriminate curettages which are performed without the exclusion of such conditions as displacements, tumours and adnexal disease."

In his remarks on sterility Dr. Solomons says: "There are two operations which we have nearly entirely discarded when treating sterility, one is curettage, the other posterior division of the cervix." He further points out the belief indulged in by "many ignorant doctors and patients that curettage is a certain cure for sterility." The writer is in full accord with these views and gave expression to them many years ago. Dr. Solomons might have added to his sound doctrine a fact not sufficiently recognized that scar tissue, incapable of renewed growth of endometrium, is often a result of curettage. The examination of the tubes by Rubin's method in the diagnosis of sterility finds its proper place in the book, the final chapter of which is on radium and X rays in gynæcology by Dr. Walter Stevenson, a concise and valuable contribution.

This book may well be recommended to students and general practitioners. It is not an academic treatise, but a practical work which shows the essentials of gynæcological practice in a clear light and with a sense of conservatism too often disregarded both in the theory and practice of the speciality.

[1] "A Handbook of Gynæcology for the Student and General Practitioner," by Bethel Solomons, B.A., M.D. (Univ. Dublin), F.R.C.P.I., M.R.I.A.; Second Edition; 1925. London: Baillière, Tindall and Cox. Demy 8vo., pp. 317, with illustrations. Price: 12s. net.

TREATMENT BY MANIPULATION.

THE small book entitled "Manipulative Surgery," by Mr. Timbrell Fisher, is on an important and yet very difficult subject, full of pitfalls. It is in effect a treatise on what in England is called "bone setting" in the hands of quacks. The author, however, is a hospital surgeon of high standing. He recognizes that quacks have often cured patients who have received no benefit from qualified men, and he points out some reasons.

At one time it was customary for surgeons to use violent movements with little or no discrimination in all sorts of cases of stiffness following traumatism while the patient was under anæsthesia. The results were occasionally extremely good, producing immediate recovery; they were usually poor and not infrequently made the patient worse. In recent years the pendulum has swung too much to the opposite extreme and violent movement has met with an indiscriminate taboo. Those who have seen the brilliant results sometimes attained by forcible movement, cannot agree with the unconditional abandonment of such methods, but will admit that in certain cases the patient may be made worse and that judgement is difficult.

Mr. Timbrell Fisher writes as an optimist. He is quite convinced as to the usefulness of carefully planned and skilfully executed passive movements in many cases of disablement. He has good and reasonable grounds for his advocacy of the methods described, methods often misused and therefore unfairly discredited. He endeavours to trace the indications for such treatment and gives directions as to methods. Judgement is indeed difficult. It is often impossible to guess very closely the conditions present, therefore working theories are liable to fail and hopes to prove futile. Mr. Timbrell Fisher makes no mention of mistakes he has made and reverses he has met with in his own practice, though we can be sure he has made mistakes and met with reverses. If he had not any such experiences, he would not have been able to write such a useful little book.

MICROSCOPY FOR BEGINNERS.

MICROSCOPY is so important in modern medicine and often so indifferently practised that any book which will tend to secure the best results from a microscope is welcome. Scales's little book,[2] "Practical Microscopy," is an adequate introduction to the subject and the matter is accurately presented except that the author leaves the impression that dark ground work is done exclusively with immersion objectives. We should like to have had for the benefit of the beginner a short historical summary of the development of the compound microscope, an explanation with illustrations of what the microscope can do and the optical theory (Chapter VI.) might well have been put at the start (Chapter II.). We must confess also that we greatly prefer lettered or numbered diagrams to photographs in a work of this nature. These, however, are minor defects. The book will be found very useful and trustworthy.

[1] "Manipulative Surgery: Principles and Practice," by A. G. Timbrell Fisher, M.C., F.R.C.S. (England); 1925. London: H. K. Lewis and Company, Limited. Demy 8vo., pp. 176, with illustrations. Price: 7s. 6d. net.

[2] "Practical Microscopy: An Introduction to Microscopical Methods," by F. Shillington Scales, M.A., M.D., B.Ch. (Cantab.); Third Edition; 1926. London: Baillière, Tindall and Cox. Crown 8vo., pp. 342, with illustrations. Price: 8s. 6d. net.

The Medical Journal of Australia

SATURDAY, JULY 24, 1926.

Some Figures and their Significance.

IN a recent issue the record for 1925 of the notifiable diseases and of the deaths from these diseases was published. It is obvious that the number of notifications of each notifiable disease does not correspond to the actual number of infections. Some persons do not seek the aid of a medical practitioner during illness. Some medical practitioners are careless in regard to their duty of notifying all attacks of notifiable diseases immediately the diagnosis is made. The diagnosis is at times missed in good faith. In the last place other diseases may simulate a notifiable infective disease so closely that a wrong diagnosis appears to be justifiable. Notwithstanding these four sources of error, the figures may be accepted as approximately accurate and comparisons with the figures of other years can be drawn. The probability of serious error becomes great if the figures of two years widely separated are compared. Several interesting facts can be noted in the table. In the first place the incidence of enteric fever is considerably lower than it was five years ago. In 1917 there were 2,740 enteric infections notified in the Commonwealth. The maximum was reached in 1920 when it was 2,995. In 1922 the figure was 1,926 and in 1925 it was 1,359. The case mortality, on the other hand, tends to be higher. In 1917 it was 10·4%; in 1918 it was just under 10·4%; in 1922 it was 11·75% and in 1925 it was 12·5%. In New South Wales the incidence fell in 1918 and 1919, but rose again in 1920 to the same level as in 1917. A substantial fall was registered in 1922 and the level in 1925 was much lower than in the previous years. In Victoria the rise in 1920 and 1921 was considerable, but the level was not so high as in 1917. The subsequent fall has been steep. The same type of curve is obtained when the figures for Queensland and the other States are plotted. It is difficult to interpret these figures. It may be assumed that the infection can be controlled by properly constructed sewerage systems and well guarded catchment areas of the water supply beds. A reduction of the incidence amounting to as much as 25%, followed by a rise to the former level within one year, cannot be explained on the basis of an improvement in sanitation. If the fall and rise of the curve in the five years from 1917 to 1921 are independent of sanitary control, it is by no means certain that the subsequent fall to the present relatively low level is the result of better administration of the sanitary laws or of greater vigilance of the health authorities. It is probable that the improvement is temporary and is due to one of those ill-understood phenomena which lead to a disturbance between the virulence of the infecting agent and the resistance of the community. In any case the health authorities should regard the improvement not so much a source of satisfaction as a reason for renewed effort to check further infections.

The incidence of scarlet fever has remained more or less at the same level for several years. There have been variations, but these variations are well known. The case mortality in 1925 was 1%.

The story of diphtheria is very different. The figures for the Commonwealth reveal frequent epidemics. In 1917 the notifications numbered 13,607; in 1918 the incidence rose to over 19,000; it fell in 1919 and 1920, but rose to a very high level, 23,192, in 1921. The year 1925 yielded a low figure, namely 7,871. If the position in the several States be examined, it will be seen that the epidemic years do not correspond. For example 1917, 1918, 1920 and 1921 were years with high incidence in New South Wales; 1918, 1919 and 1921 were epidemic years in Victoria. The case mortality seems to be strangely fixed at or about 3·5%. One fact stands out in bold relief. Both the number of notifications and the number of deaths in 1925 are much lower than the corresponding figures for any of the years between 1917 and 1922. This fact has reference to all the States. In view of the want of uniformity of the health laws in the six States and of the divergence of the methods of administration of the health laws by the health authorities, it seems un-

likely that the improvement is due to any measures of attack on the sources of infection. It is true that much attention has been directed in recent years to the prophylaxis of diphtheria and it is therefore within the bounds of possibility that the improvement is in part due to earlier diagnosis by the general practitioners with consequent earlier isolation and effective treatment. Too much may not be expected of any deliberate attack on the disease within the past year or two in Australia. The Bendigo experiment, with its clear lesson incisively taught by Dr. K. R. Moore, has not been followed by a general application of the Schick test and the immunizing of susceptibles at schools. The reduction from twenty-three thousand to seven thousand infections in the course of five years cannot be ascribed to a wholesale protection of susceptible school children. Sufficient information is not available to account for this large fall in the incidence of the disease. The cause should be sought, for its discovery may be of paramount importance to Australia.

The information concerning the incidence and fatality of pulmonary tuberculosis is meagre. It appears from such figures as are available that the disease is neither more nor less common. Approximately three thousand persons die each year from it in the Commonwealth. This figure represents about 0·05% of the total population. The table tells us that the efforts of the public health authorities are not crowned with success. Are those efforts well directed? Is the failure due to the parsimony of the governments? Has the community awakened to the seriousness of the problem and to its urgency? No sum of money would be too large if its expenditure could insure a great reduction in the incidence of this fatal disease.

There are many other interesting facts to be culled from the table, but it is impossible to find space for them all. Mention should be made of the high incidence of morbilli in South Australia. The year's figure, 14,785, is enormous and demands careful and immediate investigation. The low mortality of the disease of 3‰ should not be pleaded as an excuse for allowing this unfortunate occurrence to pass unheeded.

Current Comment.

BURNS.

THE subject of the pathological effects of burns has by no means been exhausted. Death may occur and be due to shock and in these circumstances the changes taking place in the body are those commonly associated with this condition. If the patient survives the shock, the subsequent symptoms depend naturally on the degree and extent of the burns. The clinical picture is that of a toxæmia; the symptoms usually make their appearance in twenty-four hours and may assume so serious a form that recovery is impossible. Some of the views held in regard to what actually happens in cases of burns, have been referred to in this journal on a previous occasion.[1] Pfeiffer held that death was caused by autointoxication due to destruction of protein tissue by the burning process and to the subsequent absorption of toxins. Jona also carried out some important observations by injecting extract of burned muscle into animals.[2] He found that the symptoms produced were similar to those following the injection of bacterial emulsions or extracts. Kotzareff in 1922 produced evidence to show that antibodies are formed which annul the effect of the toxic bodies produced by the burning. He advocated the systematic preparation and use of an antiburn serum.

It has been known for some time that extensive superficial burns produce lesions, sometimes minute hæmorrhages, in the cortex of the suprarenal body. These changes are progressive for several days following the burning and are most prominent in delayed death from the injury. This fact has been brought into prominence in an interesting contribution on the pathological effects of burns by Dr. H. M. Greenwald and Dr. H. Eliasberg.[3] They report two fatal cases of first degree burns in children in which unusual changes were present in the blood sugar content. The first patient was a child, aged two years. On the day following the burning chemical examination of the urine revealed an entire absence of sugar. A distinct odour of acetone was present in the breath. The child died in spite of the fact that glucose was given intravenously in a 10% solution and 0·48 mil of a one in a thousand solution of adrenalin chloride was given subcutaneously every two hours. The second patient, aged three years, was admitted to hospital five days after being burned. An odour of acetone was present in the breath and the child died in spite of an attempt at the exsanguination and transfusion treatment of Robertson and Boyd. No sugar was found in the cerebro-spinal fluid just before death and the sugar content of the blood immediately after death was less than thirty milligrammes per hundred cubic centimetres of blood. In neither case was an autopsy obtained. These findings are quite different from those of Underhill who found not only

[1] THE MEDICAL JOURNAL OF AUSTRALIA, June 16, 1923.
[2] *Ibidem*, November 3, 1917, and March 2, 1918.
[3] *The American Journal of the Medical Sciences*, May, 1926.

hyperglycæmia, but also increased concentration of the blood in a series of patients suffering from burns. Dr. Greenwald and Dr. Eliasberg point out that the latter fact would lead observers to expect an increase in the blood sugar. They came to the conclusion that in addition to the disturbance of water metabolism, as shown by Underhill, there is also a definite disturbance in the organs concerned in the regulation of the blood sugar levels. In order to study this point they carried out a series of experiments on rabbits.

In these experiments the animals were anæsthetized and burns were produced. The blood sugar content was determined at regular intervals and after death of the animal the liver, suprarenal bodies, the pancreas and some muscle tissue were removed for examination. The organs of a normal animal were used as a control. It was found that a rise in blood sugar occurred in all the animals soon after the burning. The rise began half an hour after the infliction of the burn and reached its peak as a rule one and a half hours later. The greatest rise occurred in the animals which were most severely burned and which suffered most severely from shock. When the blood sugar content was high and the rise occurred very suddenly, death as a rule followed. In three rabbits out of the ten a fall occurred after the initial rise and a secondary rise took place immediately before death. All the animals died in a state of hyperglycæmia and none in a state of hypoglycæmia. On histological examination it was found that no conclusions could be drawn from any microscopical changes found in the liver in relation to the blood sugar content. A normal glandular structure was found on examination of the pancreases. The islands of Langerhans were present in normal numbers and without changes except in two instances in which they were seen to be enlarged. These findings are of interest when considered in conjunction with Jona's experiments. It will be remembered that when Jona injected into animals extracts of muscle which had been heated to 200° C., a definite inhibitory effect was produced on the activity of secretin in inducing a secretion of pancreatic juice. It was in the suprarenal bodies that the most pronounced changes were found. In those animals which died within three or four hours after the burning, increased cellular activity was found. Only in those animals which survived the initial shock and lived for a period of from twenty-four to forty-eight hours, were degenerative changes found; accompanying them there was always some evidence of regeneration. These findings are different from those described in textbooks in that no hæmorrhage into the tissue of the suprarenal body was found and no destruction of tissue.

Reference is made to work by Belford who found that increased amount of adrenalin in the blood caused by shock was accompanied by hyperactivity of the suprarenals and was not simply the result of a release of epinephric material stored in the glands. The findings in three rabbits confirmed these observations.

As a result of their observations Dr. Greenwald and Dr. Eliasberg divided the animals into two groups. The first group comprised animals which died shortly after the burn before any considerable amount of toxic material could be absorbed and could produce any degenerative changes in the body. In these cases the high blood sugar content was regarded as being due to changes in the sympathetic nervous system resulting from shock. Changes in the innervation of the suprarenals probably caused a stimulation of the secretory functions of these glands and an outpouring of epinephrin into the circulation. In two animals of this group the glycogen content of the liver was low and in a third animal, although the glycogen content of the liver was not reduced, there was a considerable decrease in the glycogen content of the muscle. The second group described by these observers comprises animals which did not die until at least twenty-four hours or more had elapsed after the burning. This group included those with a low blood sugar level and those with a temporary hypoglycæmia. It is at this stage that destructive changes are found in the suprarenals. Dr. Greenwald and Dr. Eliasberg regard it as quite probable that because of these changes a decreased amount of adrenalin is thrown into the blood stream, thus inhibiting the liver in its normal glycogenolytic function. They regard this view as being supported by the fact that animals dying in this state manifest a higher liver glycogen content. At the same time it seems unlikely to them that death at this stage was due solely to the changes in the suprarenals.

The results of their experiments are applied by Dr. Greenwald and Dr. Eliasberg to burns in man. Their division of deaths in human beings into those due to shock and those occurring after a longer period on account of degenerative changes in the parenchymatous organs is not new. They hold that if their animal experiments are applicable to man, the use of adrenalin is contraindicated during the stage of initial shock, for it was at this time that they found hyperfunction of the suprarenals in rabbits. They propose to undertake further experiments to substantiate this view. They point out that when degenerative changes have occurred in the suprarenals and have probably caused a diminution in adrenalin secretion, the use of adrenalin in large and frequent doses is indicated. It will be seen that the clinical picture in the two patients already referred to was not what would be expected in the light of the animal experiments. The two patients died in a state of hypoglycæmia, none of the animals did so. It seems quite probable that there exists, as Dr. Greenwald and Dr. Eliasberg conclude, a parallelism between the functional state of the suprarenals and the blood sugar content, but this undoubtedly does not tell the whole story. The observations here recorded have dealt with but one aspect of the problem. Further research may possibly serve to determine what part is played by the suprarenals and the liver and what part is played by such mechanisms as antibody formation postulated by Kotzareff.

Abstracts from Current Medical Literature.

SURGERY.

Post-Operative Treatment for Ulcer of the Stomach and Duodenum.

GEORGE B. EUSTERMAN (*Surgery, Gynecology and Obstetrics*, February, 1926) in a symposium on the care of the handicapped surgical patient, deals with the treatment following operation on ulcers of the stomach and duodenum. It is very important to make a careful preoperative examination, to assess properly the advantage likely to occur to the patient and to decide from the type of individual and a painstaking estimate from the history and clinical and laboratory findings as to whether medical or surgical treatment is desirable. Post-operative supervision is not necessarily great in well selected cases, but it is sometimes indicated to regulate thoroughly the mode of living and eating, to correct certain habits and to eradicate infective foci. Dietetic control is essential to cure and should be demanded for at least six weeks after operation. The patient is advised to avoid highly seasoned, coarse and fried foods, condiments, tobacco, alcoholic stimulants and strong tea and coffee. To this is added the slogan: "Eat half as much and twice as long." The importance of persistent or recurring hyperacidity in cases of morbid convalescence is just being realized. It is highly probable that there is a causal relationship between hyperacidity and recurrent ulcer. There is clinical and experimental evidence that alkalis exert a healing influence. Besides their neutralizing effect alkalis decrease gastric tonus, inhibit regional spasm in the presence of ulcer and partly immobilize the pylorus. For routine purposes a combination of calcined magnesia and bismuth subcarbonate in doses of 0·6 to 0·9 gramme (ten to fifteen grains) respectively from one to two hours after meals with a quarter of a glass of milk is wise. An hour thereafter a glass of rich milk with or without another powder may be taken. The use of tobacco is particularly deleterious and should be discouraged. Sudden unusual exercise or exertion or an alcoholic debauch can cause a post-operative hæmorrhage even years afterwards.

The Nerves of the Stomach and their Relation to Surgery.

D'ARCY MCCREA (*The British Journal of Surgery*, April, 1926) writes on the recent advances in the physiology and pathology of the nerve supply of the stomach and the application of this knowledge to surgery. The anatomical distribution of the nerves of the stomach is sufficient to account for instances of reflex spasm or of incontinence of the pylorus in the case of gastric and duodenal ulcer and of spasm or of atony of the body of the stomach with duodenal ulcer. The ulcer-bearing area corresponds to the area in which the nerve branches are chiefly grouped. Local spasm with resultant anæmia is a probable cause of the chronicity of the ulcer, aided by such factors as retention and infection set up by reflex spasm. Certain of the gastric neuroses may be exactly simulated by the resection of either the vagi or the splanchnic nerves. The results of nerve stimulation and therefore of nerve irritation can imitate certain other neuroses. The nervous dyspepsias or gastric neuroses may be preulcerous and may have three sources of origin: (i.) Peripheral irritation of the nerves either locally in the stomach or remotely as in the gall-bladder or appendix, producing reflex gastric troubles, (ii.) lesions of the nerve paths and (iii.) central disorders, possibly of endocrine origin. As a logical sequence of the foregoing, operations upon the nerves are indicated in certain disorders and such operations are feasible. In animals the results can be forecast. Two operations have been suggested based upon these findings; one suited to the condition of pylorospasm and the other to that of cardiospasm. The operation of denervation consists of dividing the anterior layer of the hepato-duodenal ligament and adjoining part of the anterior layer of the gastro-hepatic omentum immediately above and parallel to the pylorus. The superior aspect of the pylorus and duodenum are then cleared by a process of gauze and scissor dissection, either with or without ligation of the right gastric artery and the nerve supply is thus effectively destroyed. The operation is short and simple and prevents reflex spasm. The operation for cardiospasm is somewhat similar. Definite organic stricture is a contraindication to the performance of these operations. Again, carcinoma may silently develope and a case has been reported.

Suppurative Diseases of the Lung Due to Foreign Bodies.

CHEVALIER JACKSON (*Surgery, Gynecology and Obstetrics*, March, 1926) points out the essential differences in the clinical history and the prognosis of suppurative conditions of the lung due to aspirated foreign bodies in contrast with those of other ætiology. It is remarkable that the bronchoscopical removal of a foreign body which has caused extensive suppuration of many years' duration, is followed by a comparatively rapid and complete recovery; suppuration due to other causes such as after lobar pneumonia, influenzal pneumonia, tonsillectomies *et cetera* are diffuse spreading gangrenous processes and are very resistant to treatment. Bronchiectasis of other than foreign body cause is, when well established, exceedingly difficult to cure by any medical or surgical procedure. In the presence of a foreign body the degree of suppuration is closely related to the mechanical condition, the degree and kind of obstruction. The author gives the following classifications: (i.) By-pass valvular obstruction, permitting a diminished quantity of air to pass in and out; (ii.) check-valve obstruction in which the air can get in, but has trouble to get out, this produces obstructive emphysema in the invaded lung; (iii.) stop-valve type in which the bronchus is quite closed. Metallic foreign bodies are notable for the long symptomless interval after the lodgement and the mildness of subsequent symptoms. There is no pain and little or no cough and this state is in violent contrast with the grave symptoms arising after metastatic suppuration. A long list of statistics for different types of foreign bodies presents many interesting features. Metallic substances appear to have a germicidal effect. The foreign body itself is the chief obstruction to drainage. The offending body is often walled in by a mass of granulation tissue which increases the obstruction. After removal of the foreign body, this granulation tissue largely disappears. There must be a very effective barrier to the invasion of septic organisms which is not found in the embolic cases.

The Surgical Treatment of Chronic Bacillary Dysentery.

PHILLIP MANSON-BAHR and A. L. GREGG (*The British Journal of Surgery*, April, 1926) state that chronic bacillary dysentery is a very distressing and intractable disease which has not received the surgical attention it deserves. It is caused by or is a sequel to chronic ulceration of the mucous membrane of the large intestine by the bacilli of the Flexner-Y group. The pathology of the condition is the formation of ulcers in the large bowel with serpiginous outline, undermined edges and freely communicating with lesions in the vicinity. There is a considerable formation of granulation tissue and from the resulting fibrosis the bowel wall loses its elasticity and becomes thick and rigid. The peritoneum may contain areas of nodular thickening. Large masses of polypoidal granulations bleeding readily may be present. There is an insidious onset of chronic diarrhœa with eight to ten motions per day, persisting for weeks or months. It may yield for a time to treatment, but always relapses, leading to a state of weakness, emaciation, progressive anæmia, cachexia and cardiac disturbances. Death takes place from exhaustion. Parotitis, arthritis, anæmia and toxæmic states may be complications. The diagnosis is difficult and depends on microscopical findings in the fæces, serological evidence and best of all by investigation with the sigmoidoscope. The anus is patulous and the perianal skin is atrophic. The medical treatment is disappointing. Dietetic measures should not be particularly restricted. Colonic lavage is of some value. Operation is indicated in toxæmia and failure of the lavage measures by loss of weight. Appendicostomy may be performed as a

means of relief, but caecostomy may be necessary. Caecostomy with the use of the tampon-tube supplants ileostomy, except when the small bowel is also affected. The question of closure is perplexing and the temporary closure with dressing pads assists in the decision. Stenosis of the bowel to any serious extent is rare and is localized, so that excision is possible. Tuberculous infection may be superimposed.

Carcinoma of the Lactating Breast.

EDWARD J. KLOPP (*Atlantic Medical Journal*, May, 1926) supplies a paper on carcinoma of the lactating breast. The author gives abstracts of the histories of three patients treated in the Pennsylvania Hospital and quotes eleven others collected by Schumann in 1911. Carcinoma of the lactating breast is most often mistaken for an inflammatory condition on account of its occurrence during the period of lactation. It differs, however, from inflammatory carcinoma in that the disease is seen during the later months of pregnancy or the early months of nursing. It begins as a localized area of induration which rapidly extends and involves the whole breast. The skin is dusky red or purplish red and soon attaches itself to the underlying tissues. Pain is not severe, there is no fluctuation and tenderness is not pronounced. The differential diagnosis involves consideration of mastitis, sarcoma, gumma, tuberculosis, erysipelas and X ray reactions. Of these the differentiation from suppurative mastitis is most important and in this connexion the pain is much more intense than in carcinoma and the tenderness more pronounced, the temperature is raised and a leucocytosis is present. In carcinoma the differential count frequently reveals an increase in the mononuclear cells. In regard to treatment as this form of carcinoma is a particularly malignant type of tumour, the only hope of cure lies in very early recognition. Metastases occur early and once they are established, operation is contraindicated, inasmuch as most of the patients die within a few months of operation and many manifest early involvement of the other breast. Hence the authors strongly advise the use of radium and the X rays which diminish the growth and in some cases cause the entire disappearance of the original tumour, although they cannot save the patient from succumbing to the inevitable metastases and consequent toxæmia.

Diverticulitis.

J. P. LOCKHART-MUMMERY (*The Lancet*, February 27, 1926) describes diverticulitis as occurring during the latter half of life and being due to the formation of small hernial protrusions from the lumen of the bowel through the muscular coat. These diverticula may be found in any part of the alimentary canal (except possibly the rectum), but are most common in the large intestine and particularly in the pelvic portion. The early symptoms are vague and uncertain, but the typical symptoms of a fully developed diverticulitis are attacks of pain and tenderness in some portion of the colon usually the sigmoid flexure, accompanied by a slight rise in temperature. Symptoms of chronic obstruction of the bowel accompanied sometimes by a palpable tumour closely resemble carcinoma, but the latter is not tender nor is it associated with signs of inflammation. If detected in its early stages, it may be so kept in check that surgical interference may not be necessary or may be much delayed. In its fully developed condition it is a grave disease and surgical interference is indicated before complications arise. Colostomy well away from the lesion is the safest procedure and should not be dangerous, if the diseased bowel is not too thoroughly explored or not explored at all. Resection with end to end anastomosis and temporary caecostomy is the ideal treatment according to the author whose best results have followed this procedure. As an alternative wrapping the bowel in omentum after freeing adhesions will give good results. When serious complications such local abscess, perforation into the bladder and general peritonitis have already occurred, colostomy is the only justifiable procedure.

Internal Urethrotomy.

G. P. B. HUDDY (*The British Journal of Surgery*, January, 1926) in investigating the operation of internal urethrotomy and its end results, reviews one hundred and nine cases of internal urethrotomy performed on one hundred and seven patients at the London Hospital from 1921 to 1924. In two cases the stricture recurred and a second operation was performed. The indications for the operation are: The very narrow stricture which is permeable only with difficulty and which in spite of repeated efforts will not dilate readily; the resilient stricture which dilates, but as readily contracts and the stricture in association with perineal fistula. The only absolute contraindication is complete impermeability. A two stage operation is indicated in definite urinary infection, renal insufficiency, periurethral abscess and extravasation of urine. Preliminary suprapubic cystotomy forms the first stage operation in urinary infection and renal insufficiency and free incision and drainage in periurethral abscess and extravasation of urine. The ordinary Maisonneuve operation was the one employed, followed immediately by dilatation of the urethra to its full calibre and the tying in of a number 12 catheter. The complications met with were urinary fever which may be immediate or following on the withdrawal of the catheter; hæmorrhage which was never of sufficient degree to cause alarm; atony of the bladder which rapidly cleared up on repeated catheterization; periurethral abscess and epididymo-orchitis (one case of each in the series). There was no instance of urinary extravasation. The mortality was very low, 1%, but the operations were all performed on very narrow strictures which resisted dilatation. The mortality figures when the operation was performed on strictures of wider calibre, become almost nil. The author urges that the scope of the operation should be enlarged and internal urethrotomy performed in all cases of stricture which are dilated only after some difficulty. The importance of regular postoperative dilatation cannot be too strongly emphasized. In the majority of cases, seventy-eight out of one hundred and seven, the results were excellent and the patients most gratified.

Acute Postoperative Dilatation of the Stomach.

ARTHUR J. PARKER (*Medical Journal and Record*, April, 1926) draws attention to the importance of acute postoperative dilatation of the stomach and claims that it was first recognized in 1892. It may occur after operation in any person regardless of age, sex, the operation performed and the anæsthetic used. Two main hypotheses are advanced as to its causation; one that it is a primary paralysis of the stomach due to some change in the nervous mechanism of the organ either by direct trauma or by general toxæmia; the other that the duodenum is mechanically obstructed by pressure from the mesenteric artery. The first is the most generally accepted view. The dilatation may occur at any time during the operation or during the postoperative convalescence, giving rise to vomiting, rapid pulse, difficult respiration, epigastric distention, thirst, scanty urine and terminal collapse. The vomitus is characteristic, a black brownish fluid containing black flakes. The condition most difficult to differentiate is acute high intestinal obstruction in which pain is more pronounced and distention less evident. In 1907 the death rate was reported as 92·5%, but in 1913 owing to earlier recognition and proper treatment it had fallen to 26·2%. The treatment may be prophylactic, mechanical, chemical or operative. Prevention is instituted by careful handling of the viscera and speed in operating and the adoption of the semirecumbent position after operation. Gastric lavage with warm tap water is the most important treatment and this should be repeated frequently so long as the condition persists. Strychnine, pituitary extract, atropine and morphine have all been used with doubtful effect. Saline infusions are valuable in replacing the quantity of fluid lost. After gastric lavage the most successful treatment is that of placing the patient in the prone or right lateral position with the pelvis raised.

British Medical Association News.

SCIENTIFIC.

A MEETING OF THE VICTORIAN BRANCH OF THE BRITISH MEDICAL ASSOCIATION was held in the Medical Society Hall, East Melbourne, on March 3, 1926, DR. H. DOUGLAS STEPHENS, the President, in the chair.

Non-Specific Immunity.

DR. D. MONTGOMERIE PATON read a paper entitled: "Non-Specific Immunity" (see page 103).

DR. T. S. CAMPBELL read a paper entitled :"The Non-Specific Use of Antidipheritic Serum" (see page 107).

DR. W. J. PENFOLD was satisfied that Dr. Paton's spirit of inquiry was genuine and his purpose sincere. Dr. Paton had acted on a suggestion to attempt to reproduce his results in animals. Although he had encountered a number of rebuffs, he had accepted them in the proper spirit and had persevered in his inquiry. Dr. Paton had stated in his book that he could control the reaction which ensued upon the injection of alcohol into the infraorbital nerve, by means of the oral administration of antidiphtheritic serum. He had also claimed that the tissue reaction in simple fracture could be influenced by the oral exhibition of antidiphtheritic serum. Dr. Penfold thought that he was right in saying that Dr. Paton had been unable to show that antidiptheritic serum modified either of these processes in animals. The serum had not exercised any beneficial influence upon the course of suppuration in dogs.

Dr. Penfold had informed Dr. Paton that he could not distinguish clinically between normal serum and low grade diphtheria serum apart from its specific antitoxic content. Dr. Paton had therefore carried out some experiments. Guinea pigs were injected with cultures of staphylococci; one group received diphtheria antitoxin, a second group normal horse serum and a third group normal saline solution along with the staphylococci. Generally speaking those guinea pigs which received antidiphtheritic serum in conjunction with staphylococci, exhibited much greater reaction to the injection than those which were given saline solution or normal horse serum. (Dr. Penfold suggested that this method might be of use in the standardization of the serum.) He was satisfied that the results warranted the statement that diphtheria antitoxin of low potency led to greater reaction than normal serum when injected along with staphylococci.

He confessed that he could not follow the theoretical basis upon which Dr. Paton had worked, but they had received at the Commonwealth Serum Laboratories many clinical reports similar to those recorded by Dr. Campbell in his paper. It was held by many that serum could not be of use when administered by the mouth. This was not the right attitude. Clinical observations should not be received with scepticism merely because they were at variance with prevailing notions of theoretical immunity; it behoved them rather to verify the facts and search further for the immunological explanations.

The beneficial effect of local application of serum in the treatment of ulcers had been proved. Hort who had used normal horse serum, had been the first to prove the utility of serum employed in this manner and his results had been confirmed by Grünbaum.

Dr. Campbell had advocated the use of low potency diphtheria antitoxin in severe sepsis. In this connexion Dr. Penfold would like to see a large therapeutic experiment on a controlled basis, carried out in a ward for puerperal sepsis over a period of six months, half the patients receiving the serum and half acting as controls.

Concerning the efficacy of low potency diphtheria antitoxin administered by the mouth, reports had been received at the Laboratories on the result in conjunctivitis (local instillation), arthritis, septic throats, septic conditions of the gums, alveolar abscesses and puerperal and typhoid fevers. The account of the use of the serum in typhoid fever came from Beechworth where twelve patients had been given low grade diphtheria antitoxin by the mouth in doses of a dessertspoonful every four hours. The physician in charge had stated that the temperature had fallen rapidly, the duration of the disease had been shortened and hæmorrhage had been prevented. Oral administration of serum had been used extensively in the treatment of duodenal ulcer. Serum thus given exerted a definite laxative action. In conclusion, Dr. Penfold said that the reports now to hand were such that the non-specific usage of antidiphtheritic serum merited at least a fair examination.

DR. W. O'SHAUGHNESSY said that he had employed antidiphtheritic serum in a non-specific manner for a period of nine years and that the patients he had treated now numbered more than one thousand. He had found a wide field of usefulness for the serum in acute streptococcal infections, such as erysipelas, cellulitis, osteomyelitis and septic conditions of the female pelvic viscera. He would urge its special utility in combating delayed resolution in lobar pneumonia and in broncho-pneumonia in infancy. Its most dramatic effects had been demonstrated in submaxillary adenitis.

Objections urged against the oral administration of serum were that it could not survive the action of the gastric hydrochloric acid and that it was subject to peptic digestion. To the first objection it might be answered that serum was not affected deleteriously by tricresol, 0·5% of which was added to every sample as a preservative. If the action of pepsin were a drawback, it should also operate in thyreoid medication. The manner in which the serum acted, was admittedly obscure, but the suggestion that it restored or maintained the balance of hormones appealed to him. Perhaps the best effects following the oral administration of antidiphtheritic serum were seen when it was employed in the treatment of broncho-pneumonia in infants and young children. When combined with measures to relieve the suffocative effects, antidiphtheritic serum induced a rapid amelioration in the toxæmic symptoms.

He submitted that the clinical facts could not be rejected even if they did not accord with theory. In his opinion Dr. Paton's conception that the resistance to pathological processes was only an extension of physiological resistance must be accepted.

Dr. O'Shaughnessy mentioned as an historical fact of interest that vaccines and sera were administered by the mouth to the late King Edward VII. and apparently with great benefit. The oftquoted rationale of the action of antidiphtheritic serum when given by the mouth that it depended upon the complement so supplied, was untenable in view of the great lability of complement. Perhaps the effective action of antidiphtheritic serum could be explained by the fact that the only two common pathogenic organisms which served as good antigens in provoking antitoxic response, namely the bacilli of diphtheria and tetanus, lived in the body as saprophytes and were cultivated thus in the laboratory. Such was not the case with the streptococcus, for example, which in the body was a parasite. Ordinary methods of artificial culture attempted to grow this organism as a saprophyte. He had been informed of two patients in whom anaphylactic symptoms followed the oral administration of antidiphtheritic serum.

Why was not normal horse serum equally effective? For the same reason that the peace strength of an army (a body in health) was much less than the war time strength (a body in full defensive response to antigenic attack).

DR. J. SANDISON YULE said that he had used antidiphtheritic serum in a non-specific manner extensively and in just the same types of disease as those recorded by Dr. Campbell. No one could use the serum in a large number of cases without being impressed by its efficacy. He relied on it to so great an extent in the treatment of severe sepsis that he would be in despair if he were deprived of it. He would not go so far as to say that the practitioner who used antidiphtheritic serum in the treatment of sepsis, would save every patient, but he could affirm that if the serum were employed as a routine measure a much higher proportion of recoveries would be obtained.

He wished to support Dr. Penfold in his suggestion that a big therapeutic experiment should be devised and put in operation. Would it not be possible to conduct such an experiment in the septic wards of the Women's Hospital? He was convinced of the efficacy of the oral administration of antidiphtheritic serum in severe sepsis. He could support Dr. O'Shaughnessy in his statement regarding the value of antidiphtheritic serum in the treatment of bronchopneumonia in children. He had employed it in the presence of acute osteomyelitis and was convinced that many patients had been saved from operation. The serum was also valuable in the treatment of gastric and duodenal ulcer. Of surface ulcers, such as varicose ulcers on the leg, 99% healed under the influence of antidiphtheritic serum administered orally and applied locally, often after the failure of the usual methods of treatment.

Dr. Campbell had commented on the observation that if the administration of the serum were stopped prematurely, the response when it was resumed was frequently disappointing. His experience in this respect had been identical with that of Dr. Campbell. He could testify whole heartedly to the clinical efficacy of the oral administration of antidiphtheritic serum.

DR. H. DOUGLAS STEPHENS, the President, asked what time usually elapsed before the therapeutic effect of antidiphtheritic serum given by the mouth became apparent. Mention had been made of its use in acute osteomyelitis. The course of this infection in children was very rapid and operative treatment had to be undertaken promptly if pyæmia were to be avoided. While many children affected by acute osteomyelitis were treated at first on the basis of acute rheumatism, when the action of sodium salicylate appeared, it was time to operate. Was it claimed that if such children were brought early under the influence of antidiphtheritic serum, operation might be rendered unnecessary?

He would also like to ask if Dr. Paton considered the oral administration of antidiphtheritic serum a useful measure in the treatment of tuberculosis. He assumed that any good effect derived from it would depend upon the enhanced tissue resistance it induced rather than a direct bactericidal effect upon the tubercle bacillus. Would Dr. Paton combine antidiphtheritic serum with a specific therapeutic agent?

DR. T. S. CAMPBELL in reply said that he could not speak with reference to the use of antidiphtheritic serum in the treatment of acute osteomyelitis, but he felt that it would be unwise to omit or delay operative measures. Generally speaking he had employed antidiphtheritic serum non-specifically only when he had known of no other effective treatment. In the treatment of pneumonia, for instance, he had used the serum only when he felt that the indications were that the patient was going the wrong way. He was temperamentally a disbeliever in panaceas and in spectacular results, but he had been compelled to admit that dramatic results frequently followed the non-specific use of antidiphtheritic serum. Many men of intelligence and judgement had observed the results of treatment by means of antidiphtheritic serum in their practices and it was fair that those who had opportunities for extended and controlled observations, should make them with a view to obtaining evidence in the most scientific manner.

DR. D. MONTGOMERIE PATON said that on two occasions he had treated osteomyelitis by means of antidiphtheritic serum given orally. In the first instance the patients were two sisters, aged respectively nine and eleven years. The younger was first attacked and as the diagnosis had not been made until too late, the serum had failed. The second had been treated early and had recovered. In the second instance he had been associated with Dr. J. Sandison Yule; the patient, a woman, had recovered rapidly without operation.

With reference to tuberculosis Dr. Paton said that in his opinion there was no doubt that the oral use of normal horse or sheep serum had a definite beneficial effect upon the tuberculous patient. A tuberculous suckling mother not only had her health much improved, but lactation was restored after it had ceased on account of her debility. He was greatly indebted to Dr. Penfold for his many suggestions and criticisms. With reference to the experiments mentioned by Dr. Penfold, he might say that for eighteen months, during which period he had used more than eighty animals, he had failed to obtain any success with serum orally administered. He came to the conclusion that *herbivora* could not absorb unchanged animal protein given by the mouth.

When injections of living cultures of *Staphylococcus aureus* were made with low potency antidiphtheritic serum, normal serum and saline solution respectively, results were obtained which proved that it was the manner of introduction of the serum which made all the difference. In twenty-one animals injected with staphylococci and low potency antidiphtheritic serum strong reactions had been obtained in nineteen. Of fifteen animals injected with staphylococci and normal horse serum and a similar number injected with staphylococci and normal saline solution, only three in each series exhibited reactions. Antidiphtheritic serum, therefore, contained some element which had a definite action on staphylococci.

With regard to the difficulty mentioned by Dr. Campbell and Dr. Yule of influencing the patient after a premature cessation of serum treatment, Dr. Paton said that he took the view that the serum having taken up the duty of defending the patient, there was not the usual development of his own defensive powers. Hence when the serum was prematurely discontinued, the full force of the infection fell on his unprepared and undeveloped defences and he lost so much ground that when serum was resumed he was in much worse condition than he had been at the outset.

NOMINATIONS AND ELECTIONS.

THE undermentioned has been elected a member of the Victorian Branch of the British Medical Association:

Macmillan, Wilfred Ewart, M.B., B.S., 1925 (Univ. Melbourne), Wangaratta.

Medical Societies.

THE ALFRED HOSPITAL CLINICAL SOCIETY.

A MEETING OF THE ALFRED HOSPITAL CLINICAL SOCIETY was held at the Alfred Hospital, Melbourne, on March 30, 1926, DR. D. M. SILBERBERG, the President, in the chair.

Medical Practice Abroad.

DR. J. P. MAJOR, DR. W. S. NEWTON and MR. JOHN KENNEDY gave accounts of points of medical interest noted by them in their travels abroad.

DR. J. P. MAJOR commenced with an account of his work at Queen's Square Hospital, London, dealing particularly with the sequelæ of *encephalitis lethargica*.

A most striking feature was the prevalence of patients presenting these sequelæ, many new patients being admitted each week. The majority of them dated their original illness back to the outbreak that occurred in the spring of 1924. The most common type was the Parkinsonian and most of these patients were young. One source of trouble to the parents of many of these children was the alteration in sleep rhythm, the patient commonly being awake and restless, even noisy at night and drowsy during the day, at least the early part of it. Another frequent sequel was a change in the psychology of the patient, manifesting itself in various moral perversions, alterations in habits and so forth. Even a moderate amount of crime committed was laid at the door of this disease. Because of this the Metropolitan Asylums Board was in process of making special arrangements for these patients. One needed to see a great number of these patients to realize how disastrous an outbreak of *encephalitis*

lethargica could be both immediately and afterwards. It could fairly be said that for the time being at least syphilis as a cause of nerve disease was having to play quite a secondary part.

At Queen's Square "Lipiodol" was not being so much used as formerly in the diagnosis and localization of spinal tumours, the reasons being that a large number of such conditions could be localized accurately by other means and that according to the surgeons, "Lipiodol" made the operation site "mossy" without adding appreciably to the information.

Modern work showed the term "epilepsy" to be rather an indefinite one concerning many diseases. A process which had so often occurred before, was being repeated—a disease group was being split into its component parts. Two new types were being distinguished, pyknolepsy and narcolepsy. Pyknolepsy presented itself as a series of *petit mal* attacks. They were of excessive frequency. The disease started at full pressure, as it were, attaining its maximum intensity immediately and maintaining it persistently. Although no treatment was of the slightest avail, all patients ultimately completely recovered. Narcolepsy occurred in older people and exhibited itself usually as a series of attacks of sleep in duration lasting from half a minute to half an hour, occurring inevitably at some time during each day no matter how the patient might struggle to resist them.

Another type of narcolepsy manifested itself in attacks in which muscle tone was completely lost, the whole body subsided helplessly wherever it might be without either pain or loss of consciousness. These attacks repeated themselves.

Cases of transitional type, presenting a mixture of the previous two, were seen. Narcolepsy was also of good ultimate prognosis tending to recover in eight or ten years. Drugs were of no avail.

Dealing with other nervous diseases Dr. Major mentioned disseminated sclerosis which he found surprisingly common. As many as one hundred and thirty in-patient admissions had been made in one year. In *tabes dorsalis* the most common sign was a dissociated anæsthesia which Gordon Holmes claimed was present more or less in 99% of cases and was not to be found in any condition other than tabes or general paralysis of the insane.

At Saint Bartholomew's Hospital the ward round was on Wednesday mornings limited to the unit and to visitors, students being thereby excluded. From ten o'clock until midday patients were seen and at noon Professor Fraser and his colleagues adjourned to a laboratory in which the clinical findings and diagnosis of the condition of a deceased patient were read out and this was followed by the autopsy report. Microscopical sections of the diseased organs were on view and a general discussion on the case followed. This was always interesting and informative and doubly so when, as happened occasionally, the clinical and *post mortem* findings failed to tally.

That complex gold salt known as "Sanocrysin," first used by Professor Moelgaard, of Copenhagen, had been tried frequently of late in English hospitals. The results were not as yet conclusive. The salt was used intravenously in the treatment of pulmonary tuberculosis, it being believed to kill the *Bacillus tuberculosis* in the organism in spite of the fatty content of that bacillus and in spite of the difficulty in reaching it owing to the poor vascular supply of tuberculous tissue. A very close watch had to be kept on the recipient owing to the possibility of "Sanocrysin" shock which manifested itself firstly by an albuminuria. A special serum both prophylactic and curative had been prepared to meet this complication.

At Guy's Hospital, Hurst, Symonds and two of their colleagues met one afternoon a week for two hours. Patients were seen, each physician presenting one in turn, the other three joining in the discussion. These afternoons were also most interesting and instructive.

At Saint Thomas's Hospital under Professor Maclean all diabetics were treated in the laboratory. They had been transferred from the ordinary out-patient departments so that blood sugar estimations might be made on the spot and treatment ordered accordingly. Seasonal disturbances such as febrile catarrhal conditions influenced these diabetics for the worse.

Another very interesting clinic at Saint Thomas's Hospital was that devoted to conditions due to endocrine disturbance and controlled by Gardiner Hill. He thoroughly investigated patients from his own clinic and those sent for his opinion from other clinics. An amazing collection of fat boys and fat women, acromegalics and other types of pituitary disturbance were seen there. Although the whole study of these conditions was still in its infancy, Gardiner Hill had been getting some very promising results and this was particularly noticable in the thyreoid and pituitary disorders. Dr. Major added that one need never lack work in London. At all hospitals the members of the staff were most kind and only too ready to put any facilities in the way of a visitor for doing work or seeing work done.

MR. JOHN KENNEDY said that he had first visited the Mayo Clinic at Rochester. He remarked on the genial welcome accorded him. Dr. Brasch, he said, was an extremely able man. His genito-urinary clinic was the best organized that Mr. Kennedy had seen. Patients were examined on a special genito-urinary table with water and electric light laid on to it. A mobile X ray machine was moved from room to room by a technician and radiograms were taken with the patient in position. Dr. Brasch used the old pattern direct cystoscope, little changed since he took over from his predecessor eighteen years previously and with this he worked with amazing rapidity and accuracy. For pyelograms and ureterograms he used a 12% solution of sodium iodide, for cystograms a 5% solution of "Silvol."

The patient with pyelitis was carefully investigated for possible foci of infection and the foci, being found, were eradicated. In certain types the pelvis of the kidney was irrigated with silver nitrate and "Mercurochrome." The greatest care was exercised before a diagnosis of essential hæmaturia was made. In regard to treatment foci were removed and the pelvis of kidney was irrigated with silver nitrate and the case was reviewed again at intervals. Two patients had returned at the time of Dr. Kennedy's visit. They had been under observation for some time over twelve months, they had returned for reinvestigation and were again branded as suffering from essential hæmaturia. Dr. Brasch drew attention to the frequency of occurrence of diverticula of the bladder, revealed by the taking of cystograms. Many of these patients presented symptoms of enlargement of the prostate. Dr. Hunt operated for enlargement of the prostate under sacral *plus* abdominal anæsthesia with the patient in the extreme Trendelenburg position, the bladder was kept dry and a self-retaining retractor was used. The mucous membrane round the urethra was shelled out much in the same way as a tonsil was enucleated. He put stitches in the mucous membrane of the neck of the bladder, where, he stated, the troublesome bleeding arose; after this the hæmostatic water bag was inserted into the prostatic cavity. The theatre work of the Mayo Clinic was extremely efficient, enabling a large number of operations to be performed daily. Dr. Charles Mayo was impressive on account of the thoroughness of his abdominal work, exemplified by his care in covering up raw areas. Dr. Balfour and Dr. Judd made operations on the stomach appear very simple. In gastro-enterostomy they made a small opening only and used three rows of sutures. The rule as regards duodenal ulcers appeared to be that no operation was undertaken unless there was some very definite reason apart from the discomfort of the patient. As regards hæmatemesis Dr. Harrington drew attention to a group of cases in young people, due to chronic appendicitis. Many of these in the past had been subjected to operation for ulcer, but nothing abnormal was found. As regards stomach conditions, the stomach was carefully prepared with gastric lavage three or four days before the operation and the capacity carefully estimated. The tube was used in postoperative conditions not necessarily associated with vomiting, but when there was some distension of the abdomen with elevation of pulse and anxious expres-

sion. Dr. Balfour apparently did not commonly cauterize ulcers. As regards radiology of the stomach Mr. Kennedy said he was impressed with the accuracy of the work. Whilst at the Mayo Clinic he did not see one mistaken diagnosis, though in one case the radiologist was unable to say whether the lesion was one of chronic ulcer or of carcinoma. Dr. Adson operated on a number of patients suffering from *tic douloureux*, excising in each case the Gasserian ganglion. This operation occupied about twenty minutes. It was done under local anæsthesia and in the hands of Dr. Adson was a beautiful performance. Dr. Adson's work on the spinal cord was also very fine. He attached great importance to Queckenstedt's test, the examination of the cerebro-spinal fluid, nervous signs and "Lipiodol" localization. He operated frequently under local anæsthesia. Dr. Buie, in dealing with rectal conditions, used a special couch by means of which his patient could be placed head downwards, thus making sigmoidoscopic examinations very easy. In Chicago Mr. Kennedy had been greatly impressed with the layout of the hospitals and hospital organization generally. At Cleveland Dr. Crile cordially welcomed Mr. Kennedy as a visitor from Australia. This was apparently the goître Hospital of America. Patients were carefully graded by Crile's assistant, a patient suffering from a toxic goître being rested for some days prior to operation and being treated with lugol-digitalis, bromide or "Luminal." All operations for goître were performed in the patient's room and until the anæsthetist and assistant surgeon arrived the patient did not know that an operation was about to take place. Local anæsthesia combined with ethylene or ether was used as a rule. The patient frequently talked to Dr. Crile during the whole operation. Each operation took about fifteen minutes. Dr. Crile did not cut the infrahyoid muscles as a rule. He left a strip of the gland around the trachea. He used diathermy to maintain the patient's temperature during the course of a long operation. Dr. Crile no longer operated for carcinoma of the *cervix uteri*, these being treated with radium. The theatre work at Cleveland was perhaps the best seen by Mr. Kennedy in America.

Mr. Kennedy briefly touched on the work of many other surgeons in New York.

DR. W. S. NEWTON gave an account of his work at St. Thomas's Hospital. He had had the good fortune to work in Professor MacLean's laboratory for some three months. He was impressed with the painstaking accuracy of Professor MacLean's work. If, for instance, investigational work was being carried out, it was usual for two separate teams to be employed, working independently and for the results to be correlated to insure accuracy.

For some time he had worked in the large metabolic clinic, doing estimations of basal metabolic rates and at the same time examining the patients from the clinical aspect.

The endocrine clinic was very large, many of the patients being of the mixed type. Pituitary, thyreoid, ovarian disorders and many mixed conditions were to be seen there. The condition of the patients was thoroughly investigated. Those suffering from pituitary disorders, for instance, were invariably examined by X rays and the visual fields were plotted. Cushing's thermic test by the injection of one to two cubic centimetres of anterior lobe pituitary extract was used and watch was kept for a reaction consisting of a rise of temperature. Basal metabolic rate and blood sugar estimations are also made.

In hyperthyreoid conditions the best results were undoubtedly still obtained by operation and the choice of anæsthetic and technique bore a distinct relationship to the end result.

Only one or two men seemed to use ethylene and oxygen, though gas and oxygen was used extensively. Dr. Newton had seen in use none of the new type of gas machines which were American. The diabetic clinic was also large and patients were mainly treated in the laboratory after the diagnosis had been made. Here blood sugar estimations were invariably carried out and the diet and dose of "Insulin" altered accordingly. The majority of the patients were on "Insulin" treatment.

Pancreatic efficiency tests were also carried out in this laboratory. As regards nephritis the urea concentration test was mainly in vogue, though blood urea estimations were made in many instances, especially in surgical conditions.

In Colonel Harrison's clinic at Saint Thomas's many neurological syphilitics were under treatment and by means of thorough and persistent treatment good results were obtained in many of the parenchymatous conditions.

During his stay in England Dr. Newton had visited many of the chest hospitals and sanatoria. The main change noticed here was that the production of artificial pneumothorax had regained favour and that the type of patient suitable for this line of treatment had been more or less defined. He had also seen some of Cope's work on allergic diseases and some of the neurological work at Queen's Square and some of the blood work in Professor Gulland's laboratory at Edinburgh.

Post-Graduate Work.

POST-GRADUATE COURSE IN OBSTETRICS.

THE Melbourne Permanent Committee for Post-Graduate Work directs the attention of medical practitioners to the special course in obsterics which will be held at the Women's Hospital, Melbourne, during a fortnight commencing on August 12, 1926. A limited number of medical practitioners can be received in residence on payment of ten guineas for the fortnight. The whole work of the Hospital will be open to those attending the course, whether in residence or not. Applications for enrolment should be made to the joint Honorary Secretaries, Dr. J. W. Dunbar Hooper and Dr. Harold Dew, 12, Collins Street, Melbourne.

POST-GRADUATE COURSE IN BRISBANE.

THE following is the syllabus of the post-graduate course which has been arranged by the Queensland Branch of the British Medical Association.

Monday, August 2, 1926.

Morning: Diagnostic procedures in affections of the kidney, at the Hospital for Sick Children.
Afternoon: Antenatal demonstration at Lady Bowen Hospital.

Tuesday, August 3, 1926.

Morning: Orthopædic demonstration at the Brisbane Hospital.
Afternoon: Demonstration to be arranged by the Eye, Ear, Nose and Throat Section.

Wednesday, August 4, 1926.

Morning: Demonstration at the Hospital for Sick Children (Diphtheria, helminthology and so forth).
Lecture-demonstration on acute and chronic osteomyelitis.
Afternoon: Surgical work at the Mater Misericordiæ Hospital.

Thursday, August 5, 1926.

Morning: Demonstration on infant feeding at the Valley Baby Clinic.
Afternoon: Demonstration on diathermy at the Mater Misericordiæ Hospital.

Friday, August 6, 1926.

Morning: Demonstrations on blood testing, blood transfusion and on medical work at the Brisbane Hospital.
Afternoon: Radiographic demonstration at the Brisbane Hospital.

Correspondence.

THE AUSTRALASIAN COLLEGE OF SURGEONS.

SIR: The articles on the "Hospital Saturday Fund," the "Australasian College of Surgeons" and "Branches and Divisions" that have appeared recently in THE MEDICAL JOURNAL OF AUSTRALIA, give much food for thought and deal with subjects that are closely interrelated.

In the first mentioned article a statement is made that there is to be granted to subscribers to the "Hospital Saturday Fund" the right to claim admission to hospitals. It is pointed out that as a corollary to this public hospitals are likely to cease to run on eleemosynary lines. Hence it is possible that in the future the system under which honorary service is given to public hospitals by the medical profession will be replaced by some other system of medical attendance.

Should the honorary system be discontinued, one may naturally ask: Where are the would-be fellows of the Australasian College of Surgeons to secure their training? Indeed it is time that the whole question of surgical training was investigated by some authority or authorities on the subject.

This question is pertinent: Is the surgical training of the Australian graduate adequate or is it inadequate? Further, if it is inadequate, how can it be improved?

Assuming that the following statement in your article on the Australian College of Surgeons is true (in Australia the practice of surgery has suffered because of the limited competence of many general practitioners who do not hesitate to undertake the most difficult and hazardous operations), one may say that the training in surgery is inadequate, for one must remember that if general practitioners (especially those in the country) did not unhesitatingly tackle difficult and dangerous procedures, even though their competence may be limited, many more people would lose their lives than at present.

It is well to bear in mind that there are country surgeons who are quite as skilful as the average surgeon in the largest metropolitan hospitals, and some may have greater skill than the average surgeon holding a hospital appointment.

Most people will agree that the idea of an Australian college of surgeons is an excellent one. The results of the college as stated in the leading article will depend on wise and careful management.

To the writer it appears that it would be wise if there were a provision that the original fellows of the proposed college must be honorary consulting surgeons. Original fellows could draw up conditions governing the admission to college of those persons at present engaged in the practice of surgery and also for future medical graduates. It is to be hoped that fellows will not be required to restrict themselves to the practice of surgery (as is the case in the American College), as if this is required it will preclude and discourage many surgeons and especially those in the country from becoming fellows and it is just as important to encourage a better standard in the country as in the city, if not more important.

You point out, Mr. Editor, in your excellent article on "Branches and Divisions" many practitioners have no opportunity of meeting colleagues and discussing common problems. This should be remembered by those who are seeking to establish an Australasian College of Surgeons.

As indicated earlier the question of surgical training of Australian graduates is one that should be carefully investigated.

There is nobody in Australia who can give an authoritative opinion as to the quality of surgical work performed in each town in Australia. That the Australian graduate is most competent is an accepted fact, but judging by the remarks of some of his teachers so far as surgery is concerned, it must be in spite of his training not because of it.

It is possible that the great fault in the teaching system in Australian medical schools is that there has been no attempt to develope an Australian type of graduate; in other words the ways of older medical schools have been too slavishly followed. It would be better to train our graduates in such a manner that they will be best able to overcome difficulties that are peculiar to Australian environment.

In common with many other countries we are attempting to teach medical students too much. Medical science has made great strides in recent years, so much so that it is impossible to turn men out as general specialists. The aim should be to make them all capable of becoming competent general practitioners. To achieve this object they should have a thorough grounding in the principles of physics, chemistry and biology and anatomy.

The courses in physiology, pathology, biochemistry and pharmacology could be much shortened; much in medicine and surgery could be eliminated; more time should be spent in conditions commonly met with in general practice, for example disease of children and obstetrics *et cetera*.

The medical student should have a more thorough training in all branches of preventive medicine including the early diagnosis and early treatment of disease. Places should be made on the teaching staff of the medical schools for general practitioners of proved ability. A thorough training in psychological medicine should be insisted upon. Many members of the profession whilst denouncing quacks admit the latter treat many cases of so-called functional diseases.

It must be admitted that there are few practitioners who are trained in this important work and further that many look upon those who even mention psycho-therapy, somewhat in the manner that witches were regarded in the Middle Ages.

No man should be allowed to practice a speciality, unless he can bring evidence of at least two years in general practice. Many young men are rushing off to Europe and elsewhere to take up various specialities after twelve months' hospital work where they have for the most part been studying the end processes of disease.

For those who aspire to become surgeons there should be posts available as clinical assistants and research students. The new college of surgeons will have ample scope of its activities in this respect. At present nobody is responsible for the standards of medical education in Australia as a whole. The college of surgeons can lend its aid in bringing about this reform that is long overdue and one that will benefit both the medical profession and the general public.

Yours, etc.,
E. S. MEYERS,
Honorary Surgeon to In-Patients,
July 10, 1926. Brisbane Hospital.

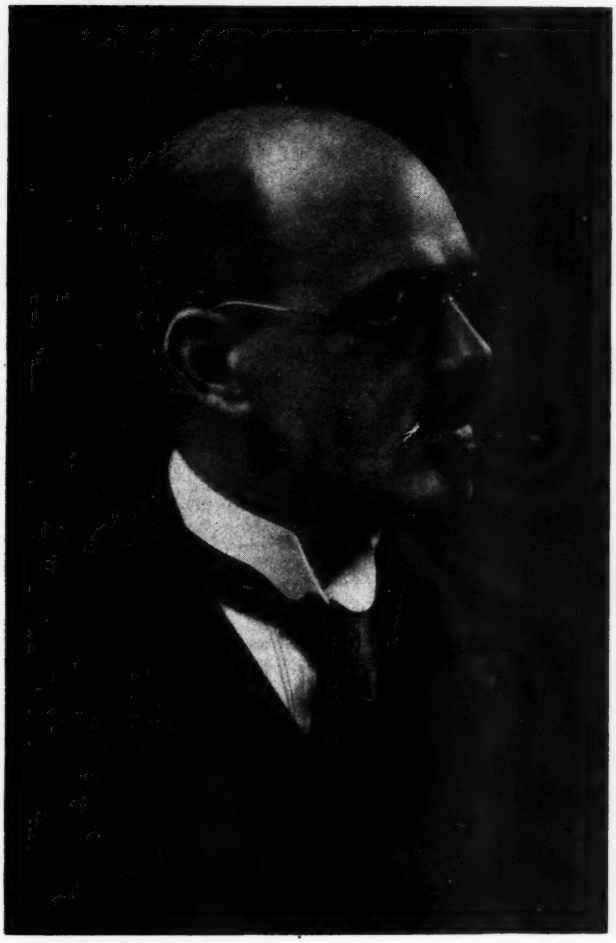
Obituary.

FRANK ANDREW.

ON June 7, 1926, Dr. Frank Andrew went on board his yacht and sailed across Corio Bay. During the course of the morning he was seized with an attack of *angina pectoris*; death ended the scene within a short time. The news of this sudden tragedy startled and shocked the whole of the medical profession in the Commonwealth and as the message was flashed across the ocean it caused deep regret among medical practitioners in other parts of the world. Frank Andrew has enjoyed a great reputation as a skilled ear, nose and throat surgeon for many years and has commanded the admiration and respect of his colleagues far and wide for his knowledge and sound judgement in scientific matters. He was not a robust man in a physical sense, yet his friends and acquaintances were totally unprepared for the news of his sudden death. It appears that in 1913 as a result of an accidental prick of his finger during an operation on a patient for empyema of the maxillary antrum he had a prolonged and critical

illness. It is probable that the pyogenic organisms that caused this illness, produced a lesion of his myocardium and thus prepared the way for his premature death.

Frank Andrew was the son of the late Henry Martyn Andrew, some time Professor of Natural Philosophy at the University of Melbourne. He was born in Sydney in the year 1881. He went to a private school in St. Kilda. He left school at the age of seventeen and secured a scholarship entitling him to enter Trinity College. He resided in Trinity and was a scholar of the College for five years. He achieved this remarkable record by securing honours at each annual examination throughout his University course in medicine. In 1903 he gained the Beaney Scholarship in Pathology and in his final year he was second in the honours list, the first place having been taken by Dr. T. P. Dunhill. He divided the exhibitions in both medicine and surgery. His contemporaries at the University of Melbourne regarded him as one of the really brilliant men of the period, a man who was destined to attain eminence in his future career.



After graduation in 1903 Frank Andrew served as a resident medical officer at the Melbourne Hospital for one year. In 1904 he was appointed resident medical officer at the Children's Hospital, Carlton. He held this position for two years. Before entering private practice he sat for and obtained the degree of doctor of medicine.

In 1906 he started in general practice in Perth. From the first he did very well. His knowledge of his professional subjects was exceptional, for Frank Andrew had the gift of memory developed to an unusual degree. He read a great deal and remembered what he read. After a short time he took up the study of the diseases of the nose, throat and ear, a specialty that had attracted him during his student days. Gradually he gave up general work in favour of this specialty. He made good use of the opportunities that were offered to a young, energetic and competent man in Perth. In those days there were few ear, nose and throat surgeons in the west. As a result his services proved extremely valuable to the community and within a short time he attained the first position in this sphere of work.

Accumulated experience and extended knowledge and skill induced him to seek a more populous centre where his ambitions might have freer play. After nine years, that is in 1915, he left Perth and set up in Collins Street, Melbourne, as an ear, nose and throat surgeon. The reputation that he had gained in Perth, followed him and he soon convinced his colleagues that his ability and erudition were much above the average. In July, 1916, he was appointed clinical assistant at the Ear, Nose and Throat Clinic at the Melbourne Hospital and two years later he was placed in charge of this clinic. For a time he practised in partnership with Dr. W. Kent Hughes. Both during this time and while practising alone his services were in great demand.

As a teacher he had few equals. Although he had never left Australia he appeared to master the teaching of all the leading authorities in otology, rhinology and laryngology and to be able to discriminate between sound doctrines and ephemeral opinions. He was a good physicist and built up his teaching of otology on secure scientific foundations. He had a quick grasp in debate, a good command of language and a ready wit, all of which tended to increase his ability as a teacher. He wrote well. He contributed some valuable papers to the Australasian Medical Congress, Brisbane, 1920, and to the Australasian Medical Congress (British Medical Association), Melbourne, 1923, as well as to many meetings of the Victorian Branch of the British Medical Association, to the Eye and Ear Section of the Branch (of which he was President in 1925) and to the Melbourne Hospital Clinical Society. Mention may be made of his work on tuberculosis of the larynx and cerebral suppuration of otic origin as typical examples of clear thought and facility of expression. He did not restrict his attention to the narrow limits of a specialty, for his remarks during debates on surgical, epidemiological and other subjects were always worthy of consideration.

During the eleven years spent in Melbourne he worked steadily and advanced in knowledge and in the opinion of his colleagues. He impressed his patients with the soundness of his knowledge and gained their confidence at all times.

He was an ardent yachtsman. His yacht was a source of pride and unalloyed delight to him. He was extremely fond of music, especially orchestral and chamber music and was a good judge of a first class performance. He was also interested in architecture.

He is survived by his widow and a son and a daughter. The sympathy of his colleagues is extended to them.

DR. STEWART W. FERGUSON writes:

To write of a very near friend and colleague on the morrow of his death must ever be the most painful and difficult of tasks. And such a task is increased tenfold when one would attempt to measure up a personality so vivid and robust and many sided as that possessed by Frank Andrew. He was altogether an outside size.

Seldom have we possessed in Australia a man so rich in parts. His surgery, unfaltering, brilliant and decisive, suggested the cold, exact mind devoted to a single professional purpose; it might suggest, too, a disposition to dwell apart from his fellows. But nothing could be further from Frank Andrew as he was. Few men ranged wider in their interests, sympathies and studies; fewer still were more companionable and lovable. He was with all his self-sacrificing devotion to his professional work essentially a man's man, a man of the world, a man of affairs. Surgery was almost a religion to him, but outside surgery he pursued many other interests with so much enthusiasm and with such an apparent singleness of thought that a stranger might well have been incredulous as to his professional eminence. In truth Frank Andrew's mental gifts were of that occasional kind that grasp and master at a flash things which take an average mind a long and wearisome time to acquire and even then are acquired imperfectly. His rare intelligence carried him as by inspiration to the heart of things. In the most intricate of surgical cases he proceeded with a degree of confidence and with an absence of effort such as only a master of his subject could display.

As is not uncommon in men to whom relative excellence in achievement is easy, Frank Andrew was sometimes criticized for his positive bearing and the bluntness with which he expressed his opinions. But if those who knew him imperfectly were occasionally abashed at his emphasis of view, he was to his friends and in his heart, as are all really big men, modest and natural. None in his profession knew better than he that he was but on the threshold of learning and achievement. To the day of his death he was a sincere and humble student.

As a friend and companion he was surely very rare. Those who, like the writer, worked for years almost daily in his company, never knew a moment that was dull and were never troubled by even a passing phase of personal misunderstanding. His naturalness and sincerity were stark and invariable. He was the merriest of men, fragrant and stimulating as the southerly winds off the sea he loved so well. He carried a frail physique with a splendid gallantry. Men and women of all classes were refreshed and heartened by his exuberance and his plain dealing. Few men have carried into middle age so many of the direct, engaging, uncorrupted qualities of boyhood.

Frank Andrew was interested in so many things outside his profession that we always marvelled as to when he found time for all the reading and observation which had so richly stored his mind. A close friend of his, who is an experienced observer of public men, has said that had Andrew turned to politics, he would have had a rapid rise to high places.

When death came to him he had his hand on the helm of his yacht. It was as he would have wished. For years he had spent his holidays buffetting in little craft on the outside ocean. At times he was captain, crew and cook. He was a great all-rounder and greatest of all as helpmate, counsellor and friend.

DR. H. HUME TURNBULL writes:

Although the whole profession of Australia realizes the great loss which medicine has sustained in the death of Frank Andrew, only those who have known him long and intimately, can appreciate all that his premature death means.

From the days of his residency at the Children's Hospital, when I first worked with him, he amazed us all by his capacity for work and work of the highest quality.

If his interest was captured by a problem he would throw himself completely into its elucidation. He thought nothing of working the greater part of the night after a long day at blood examination or other laboratory work and then recommencing his ordinary work at the usual time. If a case was interesting or critical he would toil unceasingly till the problem was solved or the corner turned and then he would pass on to the next big job, never wasting time in admiring the previous result.

He was amazingly dexterous with instruments and could examine even small children without hurting or frightening them, indeed my family looked forward with the greatest keenness to a visit from him and anyone he did not examine was very disappointed. One could always depend on his readiness to go anywhere at any time with the utmost good humour; he never seemed annoyed at being dragged out again after the longest day, but would appear quite pleased to come.

His opinion was clear and decisive and his very wide knowledge of medicine and surgery gave a breadth of outlook and understanding that made any consultation with him an intellectual treat. He was an admirable clinical teacher and could keep his instruction on a level which all intelligent students could understand, while his wide knowledge enabled him to point the general significance of special diseases in a convincing manner. His work and example were a tremendous stimulus to all who worked with him and he would take any trouble to help men who wanted to work, and he could never understand the emotion of jealousy.

He wanted every man to yield the best that was in him and took it for granted that he should be given all possible opportunities.

With it all he was a most lovable man, strong, individual and sincere and one of the most unselfish and kindest men I have ever known.

His loss is irreparable, but his influence must persist and his example of what can be done by brains and industry with no assistance at all from outside should be invaluable in these days when the cry is ever for more and more "spoonfeeding."

DR. J. H. SHAW writes:

As one of the younger men I cannot refrain from expressing my admiration for the late Dr. Frank Andrew.

To me as a student and I fancy to all students, he was unique as a teacher since he established immediately a sense of adventure in the pursuit of knowledge and a sense of comradeship, in that he himself was the greatest student of us all. Was the management of the frontal mirror baffling and elusive? Well after all it was not really difficult; his own early struggles had not been forgotten and the solution he had found would be carefully explained. And so it was with things more intricate. Having once listened to him demonstrating an acute otitis with all its possible sequelæ, the student carried in his mind for ever the cardinal points which he must be certain of, if the life of his patient were not to be endangered.

To hear him talking anatomy was to recover the enchantment of one's childhood days when "Jack the Giant Killer" and "Little Red Riding Hood" were really true adventures to be lived through in every moment of their telling.

Returning from post-graduate work in England and on the continent I was stimulated beyond measure by his brilliant mind. "Ruttin and Alexander thought so and so, did they? Well, yes; but had they considered it from this point of view?" And then would flow a wholly original and fascinating reconstruction of the problem, illustrated every now and then by clinical data from the wide resources of his own experience.

There can have been few intellects of his quality in the specialty, still fewer possessing so retentive a memory. A paper by Alexander, read in German at least twelve years ago, on the histological minutiæ of the anatomy of the inner ear was still to him fresh and vivid knowledge ready for instant use in the solution of a difficult clinical case. Of his wide range in general medicine it is superfluous to speak. Few consultants had so much to give and few could give it so helpfully.

For the man and his friendship, as of all personal relationships, it is difficult to speak. He was not, nor ever pretended to be, all things to all men, but his confidence once gained and his friendship given there were very few grounds upon which it would be forfeited. Generous to a fault and generous far beyond the limits of his own interests, he often was to younger men and thus it is perhaps that he would have us remember him.

CHARLES KINNAIRD MACKELLAR.

WE regret to announce the death of Sir Charles Kinnaird MacKellar which occurred at Sydney on July 14, 1926.

University Intelligence.

THE UNIVERSITY OF SYDNEY.

AT a meeting of the Senate of the University of Sydney, held on July 5, 1926, an address of thanks and a commemorative medallion were received from the Faculty of Medicine of the University of Lisbon, which it was decided to acknowledge with grateful thanks.

The Honorary Secretary of the Empire Press Union advised that it had been decided that the surplus remaining to the credit of the fund established in connection with the visit of the Imperial press delegation to Australia in 1925 should be equally divided between the Australian universities, for the specific purpose of purchasing books to assist in the education of journalists. A cheque for £97 16s. accompanied the communication for which the Senate decided to express grateful thanks to the organization for its generous gift.

The Director of the Division of Studies of the Rockefeller Foundation, New York, advised that the Foundation had approved in principle cooperation with the Australian universities and scientists in the study of primitive peoples and had decided to make appropriations to the Australian National Research Council any amount equal to sums contributed from other sources, the contribution of the Foundation, however, not to exceed 20,000 dollars per year, the commitment to extend over a period of five years. It was decided to reply expressing appreciation of the allocation made and to suggest that the Advisory Council in conjunction with the Department of Anthropology should make the recommendations as to the allocation of the funds.

Dr. T. R. Pearce was appointed Demonstrator in Physiology as from July 6 and Dr. I. D. Miller was appointed Demonstrator in Anatomy for Trinity and Michaelmas Terms.

The annual report of the University Appointments Board for the year ended June 30, 1926, was adopted and ordered to be printed.

The Chancellor, the Deputy-Chancellor, the Vice-Chancellor, Sir Henry Braddon, Mr. Justice Ferguson, Professors Sir Henry Barraclough, H. G. Chapman, C. E. Fawsitt, J. B. Peden, E. R. Holme and Miss I. M. Fidler, B.A., were reelected members of the University Appointments Board for the year 1926-1927.

The following recommendations of the Joint Committee for the Diploma in Journalism were adopted:

1. That the work set down for the first year of the diploma course in journalism (which includes four first courses) may, if thought advisable on the part of the student, be taken in two years.

2. That the course on the history of journalism be incorporated with that of the principles and practice of journalism to form a combined course of forty-five lectures.

3. That the special courses be instituted in the year 1928 instead of 1927.

4. That the courses included in the second year's curriculum be taken in two years instead of one at the option of the student.

The following recommendations of the Professorial Board were adopted:

1. That all matriculants be in future required to supply certificates of good fame and character on similar lines to those now required from applicants for public exhibitions.

2. (*a*) That the establishment of a doctorate in the Faculty of Dentistry be approved, provided that the doctorate is established in accordance with the regulations already approved by the Senate for doctorates generally. (*b*) That the title of the new doctorate be that of Doctor of Dental Science (D.D.Sc.).

3. That By-law 3 of Chapter XX. be repealed and that the following new by-law be inserted in its place:

> The Professorial Board may admit either a graduate or an undergraduate of any other university as a

matriculated student in any faculty with such status as the Board thinks proper in the circumstances.

An applicant for admission under this by-law may be required to pass such examination, if any, as the Board deems requisite in order to complete the qualification for the Faculty or status.

An applicant shall not be admitted under this by-law unless he gives evidence of his degree or status and of good conduct.

An applicant shall not be deemed to be an undergraduate within the meaning of this by-law unless he has matriculated in his own unversity after passing the examination for entrance thereto.

If an applicant has not entered upon his course for graduation in his own university, he must satisfy the Board that he intended to do so or that he resided in the State or country of his own university for at least three years immediately before passing the examination for entrance thereto, or that there was some other sufficient reason why he submitted himself for that examination instead of the matriculation examination of this University.

The following recommendations of the Conjoint Board (Children's Hospital) were adopted:

1. That Dr. R. B. Wade be appointed Lecturer in Clinical Surgery at the Children's Hospital for the year 1927.

2. That Dr. E. H. M. Stephen be appointed Lecturer in Clinical Medicine at the Children's Hospital for the year 1927.

3. That the appointment of clinical teachers at the Children's Hospital should be for a period of one year, and that the positions should be reviewed annually.

4. That the lecturers be paid salary at the rate of £50 for the course.

5. That the Conjoint Board should consider all new appointments to the honorary medical staff and also the positions on the medical staff which become vacant after the effluxion of time.

The following conditions of award for the Fellowship in Urology were approved:

1. The Fellowship is to provide a means of post-graduate training and research in urology at the University of Sydney and at the same time to advance the interests of the Royal Prince Alfred Hospital.

2. Every candidate for the Fellowship must be a graduate in medicine and must have held a resident appointment at a hospital for at least one year.

3. When a vacancy in the Fellowship occurs, the position shall be advertised by the Registrar and the Senate shall appoint a Fellow on the report of the Honorary Surgeon in Urology of the Royal Prince Alfred Hospital.

4. The Fellowship shall be a whole time appointment and the Fellow shall be wholly engaged under the supervision of the Honorary Surgeon to the Department of Urology of the Royal Prince Alfred Hospital.

5. The Fellow shall be appointed for one year, but may be reappointed for a second and third year.

6. A Fellow must undertake to serve for three years, if reappointed from year to year.

7. The Fellow shall occupy a position at the Royal Prince Alfred Hospital intermediate between the honorary surgical staff and the resident surgical staff of the Department of Urology.

8. The Fellow shall be given opportunity and encouragement to conduct original research, both clinical at the Royal Prince Alfred Hospital and experimental in a suitable laboratory.

9. The clinical work to be undertaken by the Fellow shall be at first in the out-patients' department and later in the wards of the Royal Prince Alfred Hospital.

10. During the third year tenure of the Fellowship the Fellow shall be given opportunities to perform major urological operations under the guidance of the Honorary Surgeon to the Department of Urology of the Royal Prince Alfred Hospital.

11. In the case of all work published it shall be distinctly stated it is the work of the Fellow in Urology at the Royal Prince Alfred Hospital.

12. Each Fellow shall forward to the Registrar of the University for transmission to the Senate reports as to the progress of his work every six months and the tenure of the Fellowship shall be subject to these reports being deemed satisfactory.

13. Any holder of the Fellowship shall be amenable to the same rules and regulations as those governing the resident medical staff of the Royal Prince Alfred Hospital and on committing any serious breach of such rules and regulations the Fellow may be suspended by the Honorary Surgeon of the Department of Urology, subject to an appeal to the Senate of the University.

14. The Senate may from time to time alter these regulations and may prescribe such further regulations as may be found necessary.

The following recommendations from the Faculty of Medicine were approved:

1. That the degree of M.D. be awarded to Professor J. C. Windeyer, M.B., Ch.M., for his thesis "Abdominal Methods of Obstetrical Diagnosis," and to Mr. E. S. Morris, M.B., Ch.M., for his thesis "The Causes and Prevention of Maternal Morbidity and Mortality."

2. Courses in Obstetrics:
   (*a*) That in the years when the final examination is held at the end of Trinity Term of the sixth year (as in 1927 and 1928) the main course of nine weeks' obstetrical teaching be given between June and December of the fifth year and the refresher course consisting of two weeks' residence in hospital be given between January and June in the sixth year.
   (*b*) That attendance of students be alternated so that in 1927 students from the Royal Prince Alfred Hospital go to the Royal Hospital for Women and the South Sydney Hospital for Women and students from Sydney Hospital and St. Vincent's Hospital go to the Women's Hospital, Crown Street, while in 1928 students from the Royal Prince Alfred Hospital go to the Women's Hospital, Crown Street and students from Sydney Hospital and St. Vincent's Hospital go to the Royal Hospital for Women and the South Sydney Hospital for Women.
   (*c*) That in the years when the final examination is held at the end of Michaelmas Term in the sixth year (as in 1929) the main course of nine weeks' obstetrical teaching be spread over one year from June of the fifth year to June of the sixth year and the Refresher Course be spread over six months, namely from June to November inclusive of the sixth year.

3. Fifth Year Time Table:
   (1) That the lectures in gynæcology be delivered at 8.30 a.m. daily during the last six weeks of the long vacation between the fourth and fifth years.
   (2) That the lectures and demonstrations in pharmacology be given during Lent Term of the fifth year from 10.30 a.m. to 1 p.m. on three days per week throughout the term, the treatment of the subject to be left to the teachers.
   (3) That the lectures in medical jurisprudence take place daily at 9.30 a.m. during the first four weeks of Michaelmas Term.
   (4) That the lectures in preventive medicine take place daily at 8.30 a.m. throughout Michaelmas Term.
   (5) That the classes in practical pharmacy take place throughout Trinity and Michaelmas Terms on Saturdays from 8.30 a.m. to 10.30 a.m.

4. Sixth Year Time Table:
   (1) That the lectures on special subjects take place during the long vacation between the fifth and sixth years and in Lent Term of the sixth year and that in addition to the prescribed lectures at the University the lecturers should continue to give demonstrations at the hospitals in accordance with the hospital time-tables.

(2) That these lectures commence at 8.45 a.m. except on Saturdays when the lecture in psychiatry at one of the mental hospitals should commence at 10 a.m.
(3) That the three lectures on medical ethics take place in the long vacation.
(4) That clinical pharmacology be considered along with pharmacology in the fifth year.
(5) That when the final examination is held at the end of Michaelmas Term the whole of Trinity Term together with the June vacation making twelve weeks in all be set apart for teaching work at the Royal Alexandra Hospital for Children, but that while the final is held at the end of Trinity Term six weeks only be so set apart.
(6) That teaching in infectious diseases at the Coast Hospital take place on Saturday during the long vacation.

The following recommendation of the Faculty of Science was adopted:

That the degree of D.Sc. be awarded to Mr. P. D. F. Murray, B.Sc., for his thesis "An Experimental Study of the Development of the Limbs of the Chick." Mr. Murray graduated B.Sc. in 1922 with 1st Class Honours and University Medal in Zoology and 1st Class Honours in Botany. On being awarded the John Coutts Scholarship in 1922 he proceeded to Oxford where he took the B.Sc. degree by research.

The by-laws prescribing the course for the degree of Bachelor of Science were amended.

THE UNIVERSITY OF ADELAIDE.

Revised Regulations of the Degree of Doctor of Medicine.

THE following regulations of the degree of Doctor of Medicine have been adopted by the Council of the University of Adelaide on June 25, 1926, in the place of the regulations of 1921:

I. To obtain the degree of Doctor of Medicine, candidates must have been admitted to the degree of Bachelor of Medicine in the University of Adelaide.

II. No candidate shall be eligible for examination until the ninth academic term after his admission to the degree of Bachelor of Medicine, except by permission of the Council on the recommendation of the Faculty of Medicine.

III. The candidate, unless exempted as hereinafter provided, shall pass an examination in (*a*) general medicine, including pathology, therapeutics and the history of medicine and (*b*) such one of the following groups of subjects as he may select: (i.) Diseases of the nervous system, including mental diseases, the physiology and pathology of the nervous system and the history of these subjects; (ii.) the diseases of infancy and childhood, the pathology and history of these subjects; (iii.) State medicine in all its branches, including public health and preventive medicine and the history of these subjects; (iv.) physiology and biochemistry with their application to general medicine and the history of these subjects; (v.) pathology, including pathological anatomy, bacteriology and the history of these subjects; (vi.) anatomy and histology with their application to general medicine and the history of these subjects: Provided that no candidate will be allowed to take both the M.D. and M.S. examinations in anatomy only.

IV. An examination for this degree shall be held, if required, in May and November in each year. The examination shall be conducted by means of printed or written papers, *viva voce* questions, practical demonstration and clinical examination of patients or by any of these methods. Each candidate shall forward to the registrar before the first day of February or the first day of August in any year notice of his intention to present himself for the next examination and shall state the group of subjects in which he desires to be examined.

V. The candidate shall submit with this notice a printed or typewritten thesis of his own composition on some branch of medicine or of the allied sciences and embodying the results of independent reasearch and observation. The candidate may be required to undergo an examination in the subject matter of his thesis. The thesis may be specially written for the degree or be an already published work or a paper or series of papers read before any of the recognized medical societies of Australasia or of Great Britain and the candidate shall indicate wherein he considers that it advances medical knowledge or practice and shall furnish a history of the progress of medical knowledge in the subject to the date of its presentation. If the thesis be adjudged to be of sufficient merit by the Faculty or by the examiners appointed to adjudicate upon it and if the candidate furnish evidence satisfactory to the Faculty of a sufficiently advanced knowledge of the principles and practice of medicine, he may be exempted from a part or the whole of the examination. If the thesis be not accepted, the candidate shall not be permitted to proceed to examination.

VI. The names of successful candidates shall be arranged in alphabetical order.

VII. A printed or typewritten copy of any thesis approved by the examiners shall be deposited in the library of the University before the candidate is admitted to the degree.

VIII. Schedules may be drawn up from time to time by the Faculty of Medicine, subject to the approval of the Council, (*a*) prescribing general rules for the admission of candidates during the first or second year after admission to the degree of Bachelor, but without restricting the power of the Council to grant permission in special cases on the recommendation of the Faculty (*vide* Regulation II.), (*b*) prescribing further details of the subjects mentioned in Regulation III., (*c*) prescribing the circumstances to be taken into consideration when exempting a candidate from a portion or the whole of the general examination (*vide* Regulation V.).

Any such schedules shall be published in the University Calendar as soon as possible after they are approved by the Council.

IX. The following fees shall be paid in advance:

On entry for examination	£15 15 0
For the degree of Doctor of Medicine ..	10 10 0

Schedule Under Regulation VIII. (a).

Circumstances under which the period of three years may be shortened:

If the candidate has (i.) passed the M.B., B.S. final examination with credit or (ii.) held residential or visiting office, whether honorary or paid, in any public hospital or institution approved by the Faculty of Medicine and the Council or (iii.) assisted in the teaching in this or some other University recognized by the University of Adelaide.

The Faculty shall recommend to the Council the extent of exemption in each case.

Schedule Under Regulation VIII. (b).

To be determined by the Faculty from time to time.

Schedule Under Regulation VIII. (c).

Circumstances which may induce the examiners to recommend exemption from the whole or a part of the examination:

(1) Any higher examination passed in other universities or Royal colleges.
(2) Work in connexion with a hospital or recognized medical school or laboratory.

Books Received.

A DESCRIPTIVE ATLAS OF VISCERAL RADIOGRAMS, by A. P. Bertwistle, M.B., Ch.B., F.R.C.S.Ed., and E. W. H. Shenton, M.R.C.S., L.R.C.P.; 1926. London: Henry Kimpton. Crown 4to., pp. 270. Price: 21s. net.

NERVOUS AND MENTAL DISORDERS FROM BIRTH THROUGH ADOLESCENCE, by B.Sachs, M.D., and Louis Hausman, M.D.; 1926. New York: Paul B. Hoeber, Incorporated. Royal 8vo., pp. 877, with illustrations. Price: $10·00 net.

THE CLINICAL INTERPRETATION OF THE WASSERMANN REACTION, by Robert A. Kilduffe, A.B., A.M., M.D.; 1926. Philadelphia: Lea and Febiger. Demy 8vo., pp. 217. Price: $2·50 net.

DIATHERMY WITH SPECIAL REFERENCE TO PNEUMONIA, by Harry Eaton Stewart, M.D.; Second Edition, Revised; 1926. New York: Paul B. Hoeber, Incorporated. Crown 8vo., pp. 248, with illustrations. Price: $3·00 net.

BLOOD CHEMISTRY COLORIMETRIC METHODS, by Willard J. Stone, B.Sc., M.D.; Second Edition, Revised; 1926. New York: Paul B. Hoeber, Incorporated. Royal 8vo., pp. 142, with illustrations. Price: $3·25 net.

Medical Appointments.

Dr. John Wesley Harbison (B.M.A.) has been appointed Government Medical Officer at West Maitland, New South Wales.

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The undermentioned appointments have been made in the Mareeba Babies' Hospital, Adelaide: Dr. Helen Mary Mayo (B.M.A.), Honorary Responsible Advisory Medical Officer; Dr. Frederick Neill Le Messurier (B.M.A.), Dr. Hugh Selby Covernton (B.M.A.) and Dr. Frank Howard Beare (B.M.A.), Honorary Medical Officers; Dr. Robert Henry Pulleine (B.M.A.), Honorary Consulting Oral Surgeon.

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Dr. D. S. Mackenzie has been appointed District Medical Officer and Public Vaccinator at Perth, Western Australia.

* * * *

Dr. Whitfield De Witt Henty (B.M.A.) has been appointed Acting Medical Superintendent of the Hospital for the Insane and the Receiving House, Royal Park, Victoria.

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The undermentioned have been appointed Quarantine Officers: Dr. J. S. C. Elkington (B.M.A.), Dr. C. W. Reid (B.M.A.), Dr. C. L. Park (B.M.A.), Dr. F. E. Cox (B.M.A.), Dr. M. J. Holmes (B.M.A.) and Dr. A. H. Moseley (B.M.A.).

* * * *

Dr. Randolph Yule Mathew (B.M.A.) has been appointed Honorary Bacteriologist and Pathologist to the Port Pirie Hospital, South Australia.

* * * *

Dr. Keith McEwin (B.M.A.) has been appointed a Member of the Balaklava High School Council, South Australia.

* * * *

Dr. David McDonald Steele (B.M.A.) has been appointed a Member of the Burra High School Council, South Australia.

* * * *

Dr. John Stewart (B.M.A.) has been appointed a Member of the Gladstone High School Council, South Australia.

* * * *

Dr. Sydney Ernest Holder (B.M.A.) has been appointed a Member of the Kadina High School Council, South Australia.

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Dr. Renfrey Gershom Burnard (B.M.A.) and Dr. Eric Fitzgerald Harbison (B.M.A.) have been appointed Members of the Mount Gambier High School Council, South Australia.

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Dr. Carl Hannaford Schafer (B.M.A.) has been appointed a Member of the Peterborough High School Council, South Australia.

Medical Appointments Vacant, etc.

For announcements of medical appointments vacant, assistants, *locum tenentes* sought, etc., see "Advertiser," page xx.

ALFRED HOSPITAL, MELBOURNE: Medical Superintendent.

AUSTIN HOSPITAL, HEIDELBERG: Male Junior Medical Officer (Two Vacancies).

AUSTIN HOSPITAL, HEIDELBERG: Senior Resident Medical Officer.

Medical Appointments: Important Notice.

MEDICAL practitioners are requested not to apply for any appointment referred to in the following table, without having first communicated with the Honorary Secretary of the Branch named in the first column, or with the Medical Secretary of the British Medical Association, Tavistock Square, London, W.C.1.

BRANCH.	APPOINTMENTS.
NEW SOUTH WALES: Honorary Secretary, 30 - 34, Elizabeth Street, Sydney.	Australian Natives' Association. Ashfield and District Friendly Societies' Dispensary. Balmain United Friendly Societies' Dispensary. Friendly Society Lodges at Casino. Leichhardt and Petersham Dispensary. Manchester United Oddfellows' Medical Institute, Elizabeth Street, Sydney. Marrickville United Friendly Societies' Dispensary. North Sydney United Friendly Societies. People's Prudential Benefit Society. Phœnix Mutual Provident Society.
VICTORIAN: Honorary Secretary, Medical Society Hall, East Melbourne.	All Institutes or Medical Dispensaries. Australian Prudential Association Proprietary, Limited. Mutual National Provident Club. National Provident Association.
QUEENSLAND: Honorary Secretary B.M.A. Building, Adelaide Street, Brisbane.	Brisbane United Friendly Society Institute. Stannary Hills Hospital. Cook District Hospital.
SOUTH AUSTRALIAN: Honorary Secretary, 12, North Terrace, Adelaide.	Contract Practice Appointments at Ceduna, Wudinna (Central Eyre's Peninsula), Murat Bay and other West Coast of South Australia Districts.
WESTERN AUSTRALIAN: Honorary Secretary, Saint George's Terrace, Perth.	All Contract Practice Appointments in Western Australia.
NEW ZEALAND (WELLINGTON DIVISION): Honorary Secretary, Wellington.	Friendly Society Lodges, Wellington, New Zealand.

Diary for the Month.

JULY 23.—Queensland Branch, B.M.A.: Council.
JULY 27.—New South Wales Branch, B.M.A.: Medical Politics Committee.
JULY 27.—Illawarra Suburbs Medical Association, New South Wales.
JULY 28.—Victorian Branch, B.M.A.: Council.
JULY 29.—New South Wales Branch, B.M.A.: Branch.
JULY 29.—South Australian Branch, B.M.A.: Branch.
AUG. 3.—Tasmanian Branch, B.M.A.: Council.
AUG. 4.—Victorian Branch, B.M.A.: Branch.
AUG. 4.—Western Australian Branch, B.M.A.: Council.
AUG. 5.—South Australian Branch, B.M.A.: Council.
AUG. 5.—Section of Orthopædics, New South Wales.
AUG. 6.—Queensland Branch, B.M.A.: Branch.
AUG. 10.—Tasmanian Branch, B.M.A.: Branch.
AUG. 10.—New South Wales Branch, B.M.A.: Ethics Committee.
AUG. 10.—Section of Medicine, New South Wales.
AUG. 12.—Victorian Branch, B.M.A.: Council.
AUG. 12.—New South Wales Branch, B.M.A.: Clinical Meeting.
AUG. 13.—Queensland Branch, B.M.A.: Council.

Editorial Notices.

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